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De novo asymmetric syntheses of C-4-substituted sugars via an iterative dihydroxylation strategy

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Abstract—A short and highly efficient route to various C-4 substituted sugar lactones has been developed. The key to the overall transformation is the sequential osmium-catalyzed dihydroxylation reaction of substituted 2,4-dienoates and an allylic substitution at the C-4 position. When the Sharpless AD-mix procedure is used in a matched sense for the second dihydroxylation reaction, it results in an exceedingly diastereo- and enantioselective synthesis of several C-4-substituted sugars.

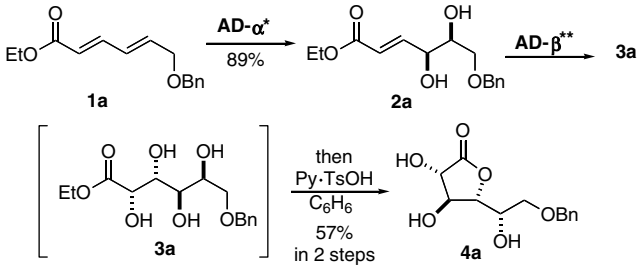
Keywords: Diastereoselective dihydroxylation; Fluorosugars; Deoxysugars; Asymmetric synthesis

1. Introduction

Over the years, considerable efforts have been made toward the development of new synthetic routes to monosaccharides.[1] The desire for these new routes was engendered by medicinal chemist's want for unnatural sugar analogues for structure activity relationship studies.[2] Of particular interest is the de novo preparation of these carbohydrates, that is, from achiral starting materials using asymmetric catalysis. The original de novo approach by Sharpless and Masamune[3] was recently taken up by McMillan (iterative aldol strategy)[4] and us (both an Achmatowicz[†,5] and an iterative dihydroxylation strategy[6–8]). Herein, we present the full account of our study of the diastereoselectivity in the second of the sequential dihydroxylations, which in turn resulted in the discovery of a concise route to several C-4-substituted sugars using the Sharpless dihydroxylation for enantiocontrol. These studies resulted in a five-step synthesis of glucono-, altrono-, and galactono-δ-lactones, via routes, which are amenable to the installation of various C-6 substituents.

2. Results and discussion

Because a bis-dihydroxylation installs a hydroxyl group at every carbon atom, it appears to be an ideal method for an efficient carbohydrate synthesis (**1a** to **3a**, Scheme 1). There were, however, issues associated with regioselectivity



Scheme 1. Enantio- and diastereoselective synthesis of galactono-γ-lactone.

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† An Achmatowicz reaction is the oxidative rearrangement of furyl alcohols to 2-substituted 6-hydroxy-2*H*-pyran-3(6*H*)-ones. For its use in de novo carbohydrate synthesis see Ref. 5.

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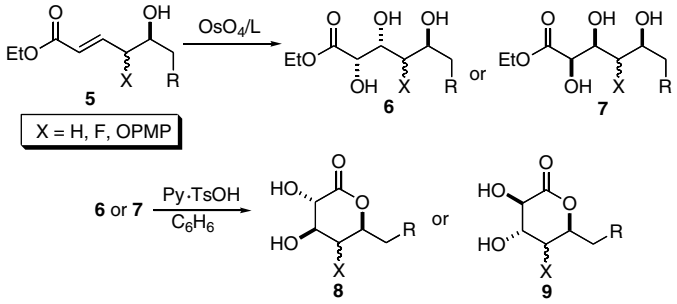


Scheme 2. Diastereoselectivity studies of C-4 substituted-δ-hydroxyenoate dihydroxylations.

(which double bond reacts first), enantioselectivity (the facial selectivity of the first dihydroxylation) and double diastereoselectivity (a balance between substrate and catalyst stereocontrol) that needed to be addressed before this concept could be put into practice.[9,10] These problems, as well as their ultimate solutions, came to light from our continuing study of the Sharpless dihydroxylation of di- and tri-enoates.[11,12] Thus, our successful strategy, outlined below, is an iterative and highly stereocontrolled oxidation of both double bonds in dienoate **1a**, which establishes all the stereocenters in galactono-γ-lactone **4a** (Scheme 1).

At the outset, we had already known that following the Sharpless protocol dienoates react with good regio- and enantiocontrol to give 4,5-dihydroxyenoates. Thus, exposing dienoate **1a** to the typical Sharpless AD-mix procedure (2% OsO_4, 2.1% $(DHQ)_2PHAL$, 3 equiv $K_3Fe(CN)_6/K_2CO_3$, 1 equiv $MeSO_2NH_2$), diol **2a** was isolated in good yield (89%) and enantiomeric excess (90% ee).[‡,13] Key to the success of this reaction sequence is that the second double bond does not react under the reaction conditions because of conflicting diastereocontrolling issues (mismatching reagent and substrate control). Consequently, when diol **2a** is exposed to the pseudo-enantiomeric reagent AD-β** (10% OsO_4, 12% $(DHQD)_2PHAL$, 6 equiv $K_3Fe(CN)_6$, 3 equiv $NaHCO_3$, 3 equiv K_2CO_3, and 1 equiv $MeSO_2NH_2$), a second matched dihydroxylation reaction occurs. After lactonization with pyridinium toluenesulfonate, galactono-γ-lactone **4a** was isolated in good yield (Scheme 1, 57%). A convenient outcome of performing two asymmetric reactions in sequence is that for all practical purposes, product **4a** is formed in both enantiomerically and diastereomerically pure form (>96% ee and de).[6b]

These results encouraged us to study the diastereoselectivity and the substrate versus reagent control that occurs in the second dihydroxylation of various C-4 substituted-δ-hydroxy enoates (e.g., **5** to **6** or **7**, Scheme 2). We were interested in gauging the effects of replacing the C-4 hydroxyl group of diol **2** with both larger (X = OPMP) and smaller (X = H) groups. Additionally, we thought that the fluoro-case (X = F) could help delineate the effect in terms of steric versus dipolar effects. We planned to prepare the C-4 substituted-δ-hydroxyenoate **5** by means of palladium π-allyl reaction (Scheme 3).[6] Unfortunately, in the fluoro case, the palladium reaction failed, so we settled for the preparation of a diastereomer via an inversion reaction (Scheme 4).

Upon applying the Sharpless AD mix-α conditions to dienoates **1a–c**, diols **2a–c** were easily synthesized in good yields (80–89%) and enantiomeric excess (80–90% ee) (Scheme 3). Diols **2a–c** were converted into cyclic carbonates **10a–c** (87–96% yield). Treatment of **10a–c** with a catalytic amount of palladium (0) source and triphenylphosphine (1 mol % $Pd(0)/PPh_3$) and a mild hydride source (3 equiv Et_3N/HCO_2H) gave the reduced alcohols **11a–c** in good yields (80–90%) and with no loss of enantiomeric excess.[§,14]

With the successful preparation of the reduced C-4-deoxy-analogues **11a–c**, we next investigated the use of oxygen nucleophiles. While many alcohol nucleophiles were investigated, only phenols gave products in good yields and with excellent regio- and stereocontrol (Scheme 3).[15] Thus, treatment of a CH_2Cl_2 solution[¶] of carbonates **10a–c** with a catalytic amount of palladium (0) (1 mol % Pd(0), 2 mol % PPh_3) and *p*-methoxyphenol as the nucleophile provided the protected alcohols **12a–c** in good yields (85–90%), with no loss of enantiomeric excess.[‖]

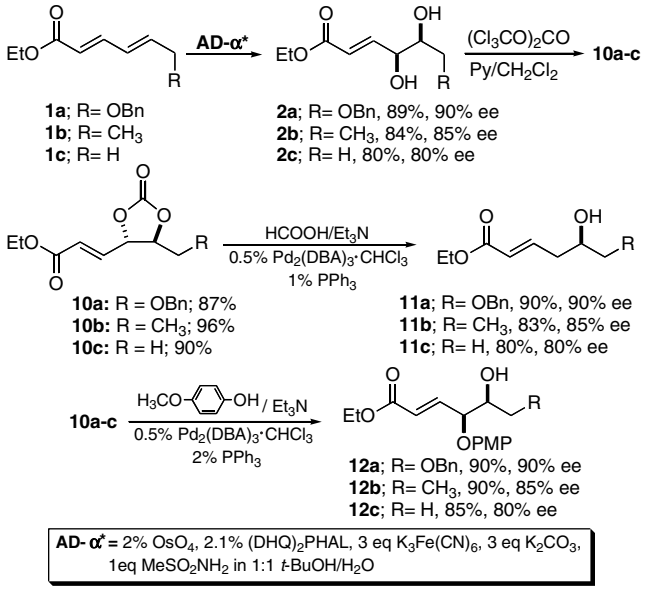
Buoyed by the success of using phenols as nucleophiles in the palladium catalyzed π-allyl reaction, we looked into the possibility of using fluoride ion as a nucleophile (**10a** to **13a**, Scheme 4). Unfortunately, we found that exposing **10a** to various fluoride sources (TBAF, HF/Et_3N, HF/Pyridine, etc.) and catalytic palladium (1 mol %; 1:2 ratio of Pd/PPh_3) failed to produce

[‡] All enantioexcesses were determined by examining the ^1H NMR and/or ^{19}F NMR of a corresponding Mosher ester.[13]

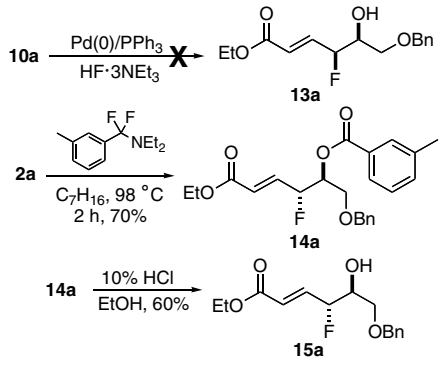
[§] It is interesting to note that the choice of THF as solvent for this reaction is critical.[14]

[¶] In contrast to the reduction reaction (**10** to **11**), CH_2Cl_2 was the preferred solvent for these reactions.[6]

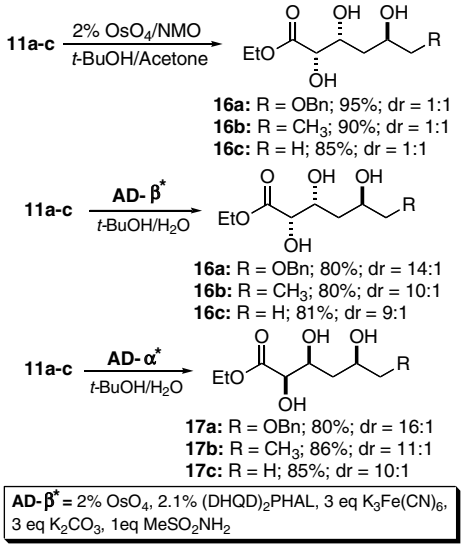
[‖] We have found that this reaction works for various phenols; however, simple alcohols (e.g., benzyl alcohol) did not participate in this reaction.



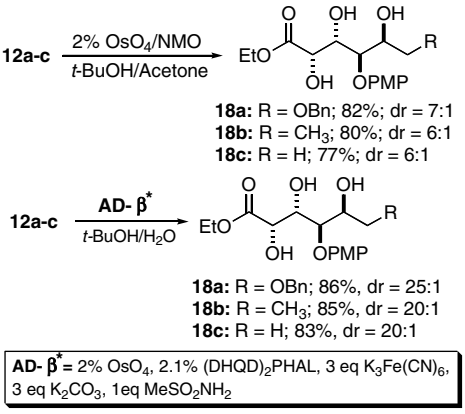
Scheme 3. Enantioselective synthesis of C-4-substituted-δ-hydroxy-enoates.



Scheme 4. Diastereoselective synthesis of C-4-fluoro-δ-hydroxyenoate **15a**.



Scheme 5. Dihydroxylation of C-4-substituted-δ-hydroxyenoates.



Scheme 6. Diastereoselective dihydroxylation of C-4 PMP-protected δ-hydroxyenoate.

13a. Typically, only a C-4 ketone product was isolated, which could have been produced via a C-5 to C-4 hydride migration.

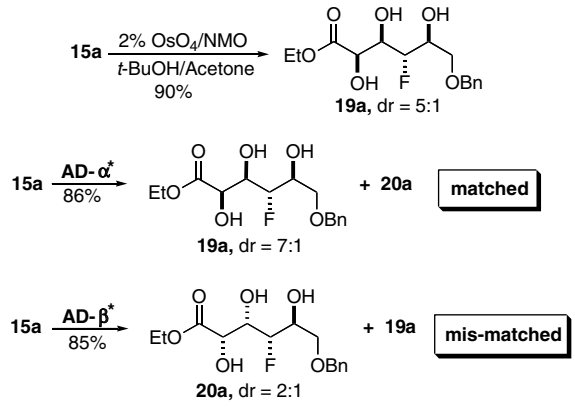
In contrast, we could easily synthesize the diastereomer of **13a** (i.e., **15a)** via a highly diastereoselective inversion reaction (**2a** to **14a**, then **15a**). Thus, when diol **2a** was subjected to *N*,*N*-diethyl-α,α-difluoro(*meta*-methylbenzyl)amine (DFMBA)[16] in heptane at 98 °C for 2 h, a C-4-fluoro-δ-benzoyloxyenoate **14a** was obtained in 70% yield with high diastereoselectivity. Deprotection of the benzoyl group with 10% HCl in EtOH afforded C-4-fluoro-δ-hydroxy enoate **15a** in 60% yield and with no loss of enantiomeric excess (Scheme 4).[13,16]

With ample supplies of several C-4-substituted-δ-hydroxy enoates (**11a**–**c**, **12a**–**c** and **15a**) in hand, we next examined the possibility of a diastereoselective dihydroxylation on the second double bond for the preparation of several sugar stereoisomers (Schemes 5–7). Thus, when alcohols **11a**–**c** were exposed to the achiral Upjohn conditions (OsO_4/NMO), 1:1 mixtures of **16a**–**c** were formed. In contrast, when alcohols **11a**–**c** were subjected to Sharpless asymmetric dihydroxylation conditions (2% OsO_4 and 2.1% $(DHQD)_2PHAL$), triols **16a**–**c** were obtained in approximately 80% yield and high diastereomeric ratios >9:1. Similarly, when alcohols **11a**–**c** were subjected to pseudo-enantiomeric Sharpless asymmetric dihydroxylation conditions (2% OsO_4 and 2.1% $(DHQ)_2PHAL$), the diastereomeric triols **16a**–**c** were formed in approximately the same yields and diastereoselectivity (~80% yield and >10:1 dr). As a consequence of performing two asymmetric dihydroxylation reactions, the major diastereomers **16a**–**c** and **17a**–**c** were isolated in essentially enantiomerically pure form (>96% ee).

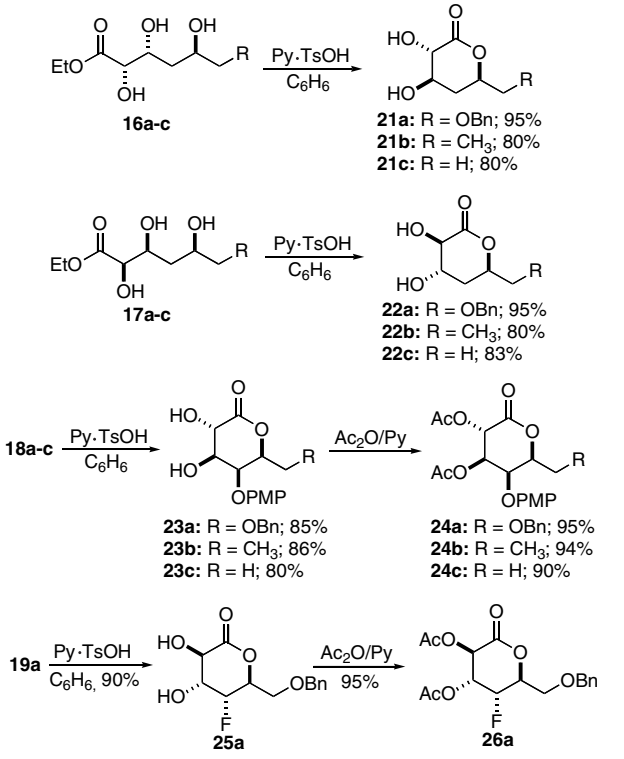
Not surprisingly, the strong substrate diastereocontrol associated with the second dihydroxylation reaction was abated with the removal of the C-4 hydroxyl group. Thus, triols **16a–c** were formed with a minor diastereomer (***ent*-17a–c**), where the formation of ***ent*-17a–c** came primarily from the minor enantiomer present in **11a–c** (***ent*-11a–c**). Once these minor diastereomers were removed by silica gel chromatography, triols **16a–c** were obtained in both diastereomerically and enantiomerically pure form (Scheme 5).

In contrast, the substrate control in the second dihydroxylation was increased when the C-4 hydroxyl group was converted into a PMP ether (Scheme 6). Thus, exposure of **12a–c** to the Upjohn conditions provided **18a–c** in improved diastereomeric ratios (>6:1) and yields (>77%). As with **2a**, PMP-ethers **12a–c** reacted in a diastereomerically matched sense with the OsO_4/$(DHQD)_2PHAL$ reagent system producing triol products **18a–c** in exceedingly high diastereomeric ratios (>20:1) and good yields (83–86%). As before, the triols, which were produced from this matched dihydroxylation sequence, were isolated in nearly enantiomerically pure form (Scheme 6).[††,10] Not surprisingly, when **12a–c** were dihydroxylated with the mismatched reagent system OsO_4/$(DHQ)_2PHAL$, poor ratios of triol products were produced.

While we were not able to prepare the directly comparable C-4 fluoride **13a**, we were able to prepare anti-diastereomer **15a**. It has been previously shown that the corresponding C-4/C-5 anti-diols exhibit poor diastereocontrol in the achiral dihydroxylation reaction.[17] In contrast to those anti-diols, much greater diastereocontrol was observed. When the 4-fluoro-δ-hydroxyenoate **15a** was subjected to the typical Upjohn procedure, they reacted with achiral OsO_4 to afford triol **19a** in 5:1 diastereomeric ratio and good yield (90%). Once again, the substrate/reagent matched effect can be seen; when *C*-4-fluoro-δ-hydroxy enoate **15a** was subjected to Sharpless asymmetric dihydroxylation reactions using the matched reagent system (2% OsO_4 and 2.1% $(DHQ)_2PHAL$), triol **19a** was obtained in good yield (86%) and increased 7:1 dr. However, when the mismatched reagent system (2% OsO_4 and 2.1% $(DHQD)_2PHAL$) was used, triol **20a** was isolated in good yield (85%) but low diastereomeric ratio (2:1) (Scheme 7).[‡‡]



Scheme 7. Diastereoselective dihydroxylation of 4-fluoro-δ-hydroxyenoates.



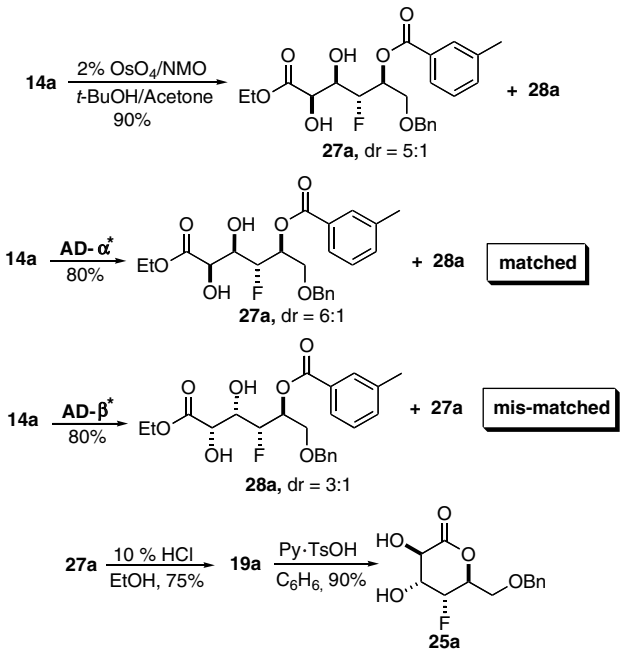
Scheme 8. Synthesis of C-4-substituted-glucono-, galactono-, and altrono-δ-lactone.

To assign the relative stereochemistry of the dihydroxylation products (**16–19**, Scheme 8), the major diastereomers were converted to the corresponding lactones and the relevant ^1H NMR coupling constants were measured. This was easily accomplished with mild acid. Thus, triols **16a–c** were converted to lactones **21a–c** in excellent yields (80–95%) upon treatment with 5% pyridinium toluenesulfonate in benzene. As with 4-deoxygluconolactones **21a–c**, the stereochemistry of **22a–c** was easily assigned from analysis of the relevant ^1H–^1H coupling constants.

Similarly, when triols **18a–c** were treated under identical conditions, galactonolactones **23a–c** were produced in 80–86% yield. At this stage, the relative stereochemis-

[††] For a discussion of the use of the Sharpless AD-mix reagent in a matched/mismatched case, see Refs. 9 and 10.

[‡‡] It is interesting to note that when **15a** reacts with mismatched OsO_4/$(DHQD)_2PHAL$ reagent, the reagent controls the stereoselectivity for the major isomer.



Scheme 9. Diastereoselective dihydroxylation of 4-fluoro-δ-benzoyloxyenoates.

try could be assigned by analysis of ^{1}H–^{1}H-coupling constants.[§§] This was easily accomplished on the diacetates **24a**–**c**, which were readily prepared using acetic anhydride and pyridine in 90–95% yield (Scheme 8). When triol **19a** was treated with 5% pyridinium toluenesulfonate in benzene, altronolactone **25a** was produced in 90% yield. At this stage, the relative stereochemistry could be assigned by analysis of ^{1}H–^{1}H-coupling constants.[¶¶] This was easily accomplished on diacetate **26a**, which was readily prepared using acetic anhydride and pyridine in 95% yield (Scheme 8).

Finally, we also investigated the diastereoselective dihydroxylation of 4-fluoro-δ-benzoyloxy enoate **14a**. Unfortunately, no improvement in diastereoselectivity was observed. Thus, when 4-fluoro-δ-benzoyloxy enoate **14a** subjected to the typical Upjohn procedure, triol **27a** in 5:1 diastereomeric ratio was produced in good yield (90%). The substrate/reagent matched/mismatched effect was also observed when 4-fluoro-δ-benzoyloxy enoate **14a** was subjected to Sharpless asymmetric dihydroxylation. Thus, when the matched reagent system (2% OsO_4 and 2.1% $(DHQ)_2PHAL$) was used, diol **27a** was isolated as the major isomer in good yield (80%) and diastereoselectivity (dr = 6:1). Similarly, the mismatched reagent system (2% OsO_4 and 2.1% $(DHQD)_2$-PHAL) produces diol **28a** in equally good yield (80%) but lower diastereoselectivity (dr = 3:1) (Scheme 9).

To assign the stereochemistry of the dihydroxylation products, the C-5 *m*-cresyl ester of **27a** was deprotected with 10% HCl in ethanol, which afforded triol **19a** in 75% yield. Subsequent conversion to the corresponding lactone **25a** was achieved in excellent yield (90%).

3. Conclusion

In summary, a highly enantio- and diastereoselective procedure for the preparation of various C-4 and C-6 substituted sugar δ-lactones has been developed. Our strategy for the synthesis of either enantiomer of these sugars provides rapid and practical access to important sugars, which should be of use for further oligosaccharide synthesis. Critical to the success of this approach was the unique use of a regio- and stereospecific palladium π-allyl reaction for alcohol differentiation and protection. When the palladium π-allyl reaction was used for a reduction, an even more flexible procedure resulted in the syntheses of 4-deoxysugars. In addition, the synthesis of 4-deoxy-4-fluoro-altrono-δ-lactone was achieved. Finally, by selecting the order in which the Sharpless reagents were used, both D- and L-sugars were produced.

4. Experimental

4.1. General methods and materials

^{1}H and ^{13}C NMR spectra were recorded on Jeol (270 MHz) and Varian VXR-600 (600 MHz) spectrometers. Chemical shifts are reported relative to internal $(CH_3)_4Si$ (δ 0.00 ppm) or $CDCl_3$ (δ 7.26 ppm) for ^{1}H spectra and $CDCl_3$ (δ 77.0 ppm) for ^{13}C spectra. Infrared (IR) spectra were obtained on a Prospect MIDAC FT-IR spectrometer. Optical rotations were measured with a Jasco DIP-370 digital polarimeter in the solvent specified. Melting points were determined with Electrothermal Mel-Temp apparatus and are uncorrected. Flash column chromatography was performed on ICN reagent 60 (60–200 mesh) silica gel. Analytical thin-layer chromatography was performed with precoated glass-backed plates (Whatman K6F 60 Å, F_{254}) and visualized by quenching of fluorescence and by charring after treatment with *p*-anisaldehyde or phosphomolybdic acid or potassium permanganate stain. R_f values were obtained by elution in the stated solvent ratios (v/v). Ether, THF, CH_2Cl_2, and Et_3N were dried by passing through an activated alumina column with argon gas pressure.

[§§] Particularly revealing coupling constants were those between the two axial protons at C-2 and C-3 (e.g., for **24a**, $J_{2,3} = 10.2$ Hz) and between the equatorial proton at C-4 and the two axial protons at C-3 and C-5 (e.g., for **24a**, $J_{3,4} = 2.4$ Hz and $J_{4,5} = 1.4$ Hz).

[¶¶] Particularly revealing coupling constants were those between the two axial protons at C-2 and C-3 (e.g., for **26a**, $J_{2,3} = 10.2$ Hz) and between the equatorial proton at C-4 and the two protons (e.g. axial at C-3 and equatorial at C-5; for **26a**, $J_{3,4} = 2.4$ Hz and $J_{4,5} = 2.4$ Hz).

Commercial reagents were used without purification unless otherwise noted. Melting points are uncorrected. Air and/or moisture-sensitive reactions were carried out under an atmosphere of argon/nitrogen using oven-dried glassware and standard syringe/septa techniques.

4.2. (*E*,4*S*,5*S*)-Ethyl 6-(benzyloxy)-4,5-dihydroxyhex-2-enoate (2a)

Into a 250 mL round bottomed flask were added 60 mL of *t*-BuOH, 60 mL of water, $K_3Fe(CN)_6$ (24.7 g, 75 mmol), K_2CO_3 (10.35 g, 75 mmol), $MeSO_2NH_2$ (2.37 g, 25 mmol), $(DHQ)_2PHAL$ (409 mg, 0.52 mmol, 2.1 mol %), and OsO_4 (127 mg, 0.5 mmol, 2 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added (2*E*,4*E*)-ethyl 6-(benzyloxy)hexa-2,4-dienoate **1a** (6.15 g, 25 mmol), and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (300 mg) at rt. EtOAc (40 mL) was added to the reaction mixture and after separation of the layers, the aqueous phase was further extracted with the organic solvent (2×30 mL). The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (7:3, hexanes/EtOAc) afforded 6.23 g (89% yield) of **2a** as a light yellow oil; R_f (30% EtOAc/hexanes) = 0.13; $[\alpha]_D^{25}$ −20.4 (*c* 1.1, CH_2Cl_2); IR (thin film): 3421, 2985, 2937, 2871, 1715, 1699, 1659, 1455, 1393, 1279, 1179, 1039, 984 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 7.33 (m, 5H), 6.91 (dd, $J = 15.6$, 4.6 Hz, 1H), 6.14 (dd, $J = 15.6$, 1.8 Hz, 1H), 4.58 (d, $J = 11.8$ Hz, 1H), 4.53 (d, $J = 11.8$ Hz, 1H), 4.38 (ddd, $J = 9.1$, 4.6, 1.8 Hz, 1H), 4.19 (q, $J = 7.1$ Hz, 2H), 3.76 (ddd, $J = 9.7$, 5.5, 4.6 Hz, 1H), 3.65 (dd, $J = 9.7$, 3.9 Hz, 1H), 3.59 (dd, $J = 9.7$, 5.5 Hz, 1H), 2.92 (d, $J = 4.7$ Hz, 1H), 2.70 (d, $J = 5.9$ Hz, 1H), 1.28 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 166.2, 146.0, 137.3, 128.5 (2C), 127.9, 127.8 (2C), 122.4, 73.7, 72.1, 71.7, 71.4, 60.5, 14.1; GCMS: 280 $[M]^+$.

4.3. (3*S*,4*S*,5*R*)-5-(2′-Benzyloxy-(1′*S*)-1′-hydroxyethyl)-3,4-dihydroxy-dihydrofuran-2(3*H*)-one (4a)

Into a 50 mL round bottomed flask were added 4 mL of *t*-BuOH, 2 mL of water, $K_3Fe(CN)_6$ (1.41 g, 4.2 mmol), K_2CO_3 (296 mg, 2.1 mmol), $NaHCO_3$ (180 mg, 2.1 mmol), $MeSO_2NH_2$ (68 mg, 0.71 mmol), $(DHQD)_2$-PHAL (66 mg, 0.08 mmol, 12 mol %), and OsO_4 (18 mg, 0.07 mmol, 10 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added a solution of (*E*,4*S*,5*S*)-ethyl 6-(benzyloxy)-4,5-dihydroxyhex-2-enoate **2a** (200 mg, 0.71 mmol) in 1 mL CH_2Cl_2 and the reaction was stirred vigorously at 0 °C for 4 h. The reaction was quenched by the addition of solid sodium sulfite (100 mg) at rt. Then the mixture was filtered through a pad of Celite/Florisil and eluted with 20 mL of 50% EtOAc/CH_3OH. The combined organic layers were dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and replaced with benzene (2 mL) and CH_3OH (2 mL). To this solution was added pyridinium toluenesulfonate (16 mg, 0.07 mmol, 10 mol %) and the mixture was heated at reflux for 3 h. The reaction was cooled to rt and after removal of the solvents in vacuo, flash chromatography on silica gel (3:7, hexanes/EtOAc) afforded **4a** as a viscous oil (108 mg, 57%); R_f (10% CH_3OH/EtOAc) = 0.53; $[\alpha]_D^{25}$ 29.3 (*c* 1.0, CH_3OH); IR (thin film): 3396, 2928, 2874, 1779, 1455, 1366, 1316, 1215, 1179, 1092, 1027, 978, 905 cm^{-1}; ^1H NMR (CD_3OD, 600 MHz): δ 7.27 (m, 5H), 4.48 (br s, 2H), 4.40 (d, $J = 8.4$ Hz, 1H), 4.37 (dd, $J = 8.4$, 7.8 Hz, 1H), 4.15 (dd, $J = 7.8$, 2.4 Hz, 1H), 3.99 (ddd, $J = 6.6$, 6, 2.4 Hz, 1H), 3.57 (dd, $J = 9.6$, 6.6 Hz, 1H), 3.52 (dd, $J = 9.6$, 6 Hz, 1H), 3.54 (br s, 3H); ^{13}C NMR (CD_3OD, 150 MHz): δ 176.3, 139.6, 129.5 (2C), 129.0, 128.8 (2C), 81.6, 75.8, 74.5 (2C), 71.9, 68.6; CIMS calculated for $[C_{13}H_{16}O_6+Na]^+$: 291.0845. Found: 291.0875.

4.4. (*E*)-Ethyl 3-((4*S*,5*S*)-5-((benzyloxy)methyl)-2-oxo-1,3-dioxolan-4-yl)acrylate (10a)

Into a 250 mL round-bottomed flask was placed 6.5 g (23.2 mmol) of **2a** in 25 mL of CH_2Cl_2 and 10 mL (116 mmol) of pyridine. The solution was cooled to 0 °C and 7.6 g (25.6 mmol) of triphosgene in 50 mL of CH_2Cl_2 was added slowly with an addition funnel. The reaction was stirred for 1.5 h and quenched by the addition of saturated aqueous NH_4Cl (40 mL). The layers were separated and the aqueous layer was extracted with ether (3×50 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate (30 mL), brine (25 mL), and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (7:3, hexanes/EtOAc) afforded **10a** as a clear, colorless oil (6.17 g, 87%); R_f (30% EtOAc/hexanes) = 0.37; $[\alpha]_D^{25}$ −54.7 (*c* 1.0, CH_2Cl_2); IR (thin film): 2983, 2938, 2908, 2872, 1806, 1721, 1665, 1496, 1454, 1369, 1304, 1272, 1174, 1111, 1032, 978 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.34 (m, 5H), 6.83 (dd, $J = 15.6$, 5.4 Hz, 1H), 6.14 (dd, $J = 15.6$, 1.4 Hz, 1H), 5.17 (ddd, $J = 6.6$, 5.4, 1.2 Hz, 1H), 4.64 (d, $J = 12$ Hz, 1H), 4.58 (d, $J = 12$ Hz, 1H), 4.46 (ddd, $J = 6.6$, 3.6, 3.6 Hz, 1H), 4.24 (q, $J = 7.2$ Hz, 2H), 3.75 (dd, $J = 11.4$, 3.6 Hz, 1H), 3.66 (dd, $J = 11.4$, 3.6 Hz, 1H), 1.30 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 164.9, 153.5, 139.7, 136.7, 128.5 (2C), 128.1, 127.7 (2C), 124.5, 79.3, 76.4, 73.7, 67.7, 61.0, 14.1; CIMS calculated for $[C_{16}H_{18}O_6+Na]^+$: 329.1001. Found: 329.1003.

4.5. (*R*,*E*)-Ethyl 6-(benzyloxy)-5-hydroxyhex-2-enoate (11a)

Into a 100 mL, round bottomed flask fitted with a condenser and maintained under nitrogen were placed 3 g (9.8 mmol) of **10a**, 50.7 mg (0.05 mmol, 0.5 mol %) of $Pd_2(DBA)_3{\cdot}CHCl_3$, 26 mg (0.1 mmol, 1 mol %) of PPh_3, and 20 mL of THF. Et_3N (4 mL, 29.4 mmol) and HCO_2H (0.902 mg, 19.6 mmol) were added and the mixture was heated at reflux for 30 min. The reaction was cooled to rt and quenched by the addition of saturated aqueous sodium bicarbonate (20 mL). The aqueous layer was extracted with ether (3×30 mL). The organic layer was washed with brine (20 mL) and dried with anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (7:3, hexanes/EtOAc) afforded **11a** as a yellow oil (2.32 g, 90%). Mosher ester analysis of this alcohol shows 90% ee; R_f (30% EtOAc/hexanes) = 0.32; $[\alpha]_D^{25}$ −3.2 (*c* 1.0, CH_2Cl_2); IR (thin film): 3472, 2981, 2934, 2903, 2867, 1715, 1653, 1454, 1392, 1368, 1319, 1269, 1207, 1166, 1096, 1042, 982 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 7.34 (m, 5H), 6.96 (ddd, $J = 15.6$, 7.2, 7.2 Hz, 1H), 5.89 (ddd, $J = 15.6$, 1.3, 1.3 Hz, 1H), 4.55 (s, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 3.96 (m, 1H), 3.52 (dd, $J = 9.5$, 3.3 Hz, 1H), 3.38 (dd, $J = 9.5$, 7.1 Hz, 1H), 2.42–2.39 (m, 2H), 2.38 (d, $J = 1.5$ Hz, 1H), 1.28 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 166.1, 144.5, 137.6, 128.2 (2C), 127.6, 127.5 (2C), 123.4, 73.5, 73.1, 68.9, 60.0, 36.0, 14.0; GCMS: 264 [M^+], 191 [M^+-CO_2Et].

4.6. (2*S*,3*R*,5*R*)-Ethyl 6-(benzyloxy)-2,3,5-trihydroxyhexanoate (16a)

Into a 25 mL round bottomed flask was added **11a** (132 mg, 0.5 mmol) followed by 1 mL of *t*-BuOH and 1 mL of acetone, and then the solution was cooled to 0 °C. To this solution 0.35 mL of 50% NMO in H_2O (1.5 mmol) and OsO_4 (2.5 mg, 0.01 mmol, 2 mol %) were added, and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (100 mg) at rt. Then the mixture was filtered through a pad of Celite/Florisil and eluted with 20 mL of 50% EtOAc/CH_3OH. The combined organic layers were dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (3:7 (v/v), hexanes/EtOAc) afforded **16a/17a** as a viscous oil (141 mg, 1:1 dr, 95% yield).

4.7. (2*S*,3*R*,5*R*)-Ethyl 6-(benzyloxy)-2,3,5-trihydroxyhexanoate (16a)

Into a 50 mL round bottomed flask were added 10 mL of *t*-BuOH, 10 mL of water, $K_3Fe(CN)_6$ (4.93 g, 15 mmol), K_2CO_3 (2.07 g, 15 mmol), $MeSO_2NH_2$ (475 mg, 5 mmol), $(DHQD)_2PHAL$ (85 mg, 0.1 mmol, 2.1 mol %), and OsO_4 (25.4 mg, 0.1 mmol, 2 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added **11a** (1.32 g, 5 mmol) and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (100 mg) at rt and stirred for 15 min. Then the mixture was filtered through a pad of Celite/Florisil and eluted with 50 mL of 50% EtOAc/CH_3OH. The combined organic layers were dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (3:7, hexanes/EtOAc) afforded 1.19 g of **16a** as a viscous oil (14:1 dr, 80% yield). Major isomer: R_f (100% EtOAc) = 0.44; $[\alpha]_D^{25}$ 11.7 (*c* 2.0, CH_2Cl_2); IR (thin film): 3470, 2982, 2953, 2927, 2867, 1732, 1454, 1396, 1370, 1299, 1260, 1212, 1096, 1027 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.32 (m, 5H), 4.56 (s, 2H), 4.31–4.21 (m, 3H), 4.13 (m, 1H), 4.08 (dd, $J = 6$, 1.8 Hz, 1H), 3.52 (dd, $J = 9.6$, 3.6 Hz, 1H), 3.42 (dd, $J = 9.6$, 7.2 Hz, 1H), 3.27 (br s, 1H), 2.77 (br s, 1H), 1.81 (ddd, $J = 14.4$, 9.6, 3 Hz, 1H), 1.68 (br s, 1H), 1.67 (ddd, $J = 14.4$, 9.6, 3.6 Hz, 1H), 1.28 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 173.2, 137.7, 128.4 (2C), 127.8, 127.7 (2C), 74.4, 73.9, 73.3, 69.3, 67.4, 61.9, 36.5, 14.1; GCMS: 298 [M^+], 281 [M^+-OH], 253 [M^+-OEt].

4.8. (3*S*,4*R*,6*R*)-6-((Benzyloxy)methyl)-tetrahydro-3,4-dihydroxypyran-2-one (21a)

To a solution of **16a** (150 mg, 0.50 mmol) in benzene (3 mL) was added pyridinium toluenesulfonate (6 mg, 0.03 mmol, 5 mol %), and the mixture was heated at reflux for 5 h. The reaction was cooled to rt and quenched by the addition of saturated aqueous sodium bicarbonate (2 mL). The aqueous layer was extracted with ether (3×20 mL). The organic layer was washed with brine (10 mL) and dried with anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (4:6, hexanes/EtOAc) afforded **21a** as a viscous oil (118 mg, 95%). R_f (100% EtOAc) = 0.33; $[\alpha]_D^{25}$ −9.4 (*c* 1, CH_2Cl_2); IR (thin film): 3420, 2927, 2921, 2869, 1740, 1453, 1367, 1231, 1177, 1096, 1026, 923 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 7.32 (m, 5H), 4.56 (s, 2H), 4.49 (dddd, $J = 10.6$, 7.9, 3.9, 3.7 Hz, 1H), 4.04 (dd, $J = 10.9$, 3.9 Hz, 1H), 3.99 (d, $J = 10.9$ Hz, 1H), 3.65 (dd, $J = 10.6$, 3.9 Hz, 1H), 3.57 (dd, $J = 10.6$, 4.1 Hz, 1H), 3.33 (br s, 1H), 2.76 (br s, 1H), 2.28 (ddd, $J = 12.4$, 4.1, 3.9 Hz, 1H), 2.11 (ddd, $J = 12.4$, 10.6, 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 172.8, 137.4, 128.5 (2C), 127.9, 127.7 (2C), 76.8, 74.1, 73.5, 71.1, 68.7, 32.1; GCMS: 252 [M^+], 145 [M^+-OBn].

4.9. (2*R*,3*S*,5*R*)-Ethyl 6-(benzyloxy)-2,3,5-trihydroxyhexanoate (17a)

Into a 50 mL round bottomed flask was added 10 mL of *t*-BuOH, 10 mL of water, $K_3Fe(CN)_6$ (4.93 g, 15 mmol), K_2CO_3 (2.07 g, 15 mmol), $MeSO_2NH_2$ (475 mg, 5 mmol), $(DHQ)_2PHAL$ (85 mg, 0.1 mmol, 2.1 mol %), and OsO_4 (25.4 mg, 0.1 mmol, 2 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added **11a** (1.32 g, 5 mmol), and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (100 mg) at rt and stirred for 15 min. Then the mixture was filtered through a pad of Celite/Florisil and eluted with 50 mL of 50% EtOAc/CH_3OH. The combined organic layers were dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (2:8, hexanes/EtOAc) afforded 1.19 g of **17a** as a viscous oil (16:1 dr, 80% yield). Major isomer: R_f (100% EtOAc) = 0.44; $[\alpha]_D^{25}$ −7.4 (*c* 1.3, CH_2Cl_2); IR (thin film): 3470, 2982, 2953, 2927, 2867, 1732, 1454, 1396, 1370, 1299, 1260, 1212, 1096, 1027 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 7.33 (m, 5H), 4.56 (s, 2H), 4.27 (q, $J = 7.1$ Hz, 2H), 4.24–4.09 (m, 2H), 4.05 (dd, $J = 7.3$, 1.8 Hz, 1H), 3.49 (dd, $J = 9.5$, 3.6 Hz, 1H), 3.40 (dd, $J = 9.5$, 7.1 Hz, 1H), 3.32 (d, $J = 7.1$ Hz, 1H), 3.13 (d, $J = 2.7$ Hz, 1H), 3.07 (br s, 1H), 1.84 (ddd, $J = 14.4$, 5.9, 3.7 Hz, 1H), 1.69 (ddd, $J = 14.4$, 3.3, 3.1 Hz, 1H), 1.28 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 172.9, 137.6, 128.5 (2C), 127.9, 127.8 (2C), 74.1, 73.6, 73.4, 71.9, 70.1, 61.9, 35.8, 14.1; GCMS: 298 [M^+], 281 [M^+−OH], 253 [M^+−OEt].

4.10. (3*R*,4*S*,6*R*)-6-((Benzyloxy)methyl)-tetrahydro-3,4-dihydroxypyran-2-one (22a)

To a solution of (2*R*,3*S*,5*R*)-ethyl 6-(benzyloxy)-2,3,5-trihydroxyhexanoate **17a** (150 mg, 0.50 mmol) in benzene (3 mL) was added pyridinium toluenesulfonate (6 mg, 0.03 mmol, 5 mol %), and the mixture was heated at reflux for 5 h. The reaction was cooled to rt and quenched by the addition of saturated aqueous sodium bicarbonate (2 mL). The aqueous layer was extracted with ether (3 × 10 mL). The organic layer was washed with brine (10 mL) and dried with anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (4:6, hexanes/EtOAc) afforded **22a** as colorless crystals (118 mg, 95%). R_f (100% EtOAc) = 0.33; $[\alpha]_D^{25}$ −14.9 (*c* 0.7, CH_2Cl_2); mp 57–58 °C; IR (thin film): 3420, 2924, 2860, 1747, 1454, 1367, 1328, 1242, 1208, 1126, 1096, 1027, 923 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.35 (m, 5H), 4.74 (ddd, $J = 9.0$, 8.4, 4.8 Hz, 1H), 4.58 (s, 2H), 4.25 (d, $J = 7.8$ Hz, 1H), 4.08 (ddd, $J = 8.4$, 7.8, 4.8 Hz, 1H), 3.69 (dd, $J = 9.0$, 4.8 Hz, 1H), 3.67 (dd, $J = 9.0$, 4.2 Hz, 1H), 3.63 (d, $J = 4.8$ Hz, 1H), 2.29 (ddd, $J = 14.4$, 9.6, 8.4 Hz, 1H), 1.99 (ddd, $J = 14.4$, 4.8, 4.2 Hz, 1H), 1.59 (br s, 1H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 173.3, 137.3, 128.5 (2C), 127.9, 127.7 (2C), 74.7, 73.6, 73.2, 71.0, 68.8, 32.7; GCMS: 252 [M^+], 145 [M^+−OBn].

4.11. (*E*,4*S*,5*S*)-Ethyl 4,5-dihydroxyhept-2-enoate (2b)

Following the same procedure as described for compound **2a** (see Section 4.2), **2b** was produced (1.18 g, 6.3 mmol) in 84% yield from **1b** (1.15 g, 7.4 mmol) as a viscous oil. R_f (30% EtOAc/hexane) = 0.26; $[\alpha]_D^{25}$ −14.0 (*c* 1.2, CH_2Cl_2); IR (thin film): 3433, 2989, 2980, 2976, 2934, 2875, 1718, 1701, 1697, 1655, 1462, 1448, 1369, 1306, 1275, 1178, 1132, 1095, 1040, 976 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 6.93 (dd, $J = 15.6$, 4.8 Hz, 1H), 6.13 (dd, $J = 15.6$, 1.2 Hz, 1H), 4.20 (q, $J = 7.2$ Hz, 2H), 4.14 (dddd, $J = 10.2$, 5.4, 1.8, 1.8 Hz, 1H), 3.48 (ddd, $J = 9.6$, 7.2, 4.8 Hz, 1H), 2.73 (d, $J = 4.8$ Hz, 1H), 2.40 (d, $J = 4.2$ Hz, 1H), 1.62 (dqd, $J = 15$, 7.2, 4.2 Hz, 1H), 1.51 (dqd, $J = 15$, 7.2, 3.6 Hz, 1H), 1.28 (t, $J = 7.2$ Hz, 3H), 0.99 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.4, 146.9, 122.3, 75.3, 73.7, 60.5, 25.9, 14.1, 9.9; CIMS calculated for $[C_9H_{16}O_4+Na]^+$: 211.0940. Found: 211.0943.

4.12. (*E*)-Ethyl 3-((4*S*,5*S*)-5-ethyl-2-oxo-1,3-dioxolan-4-yl)acrylate (10b)

Following the same procedure as described for compound **10a** (see Section 4.4), **10b** was produced (1.09 g, 5.1 mmol) in 96% yield from **2b** (1 g, 5.3 mmol) as a viscous oil. R_f (30% EtOAc/hexane) = 0.54; $[\alpha]_D^{25}$ −31.6 (*c* 1.5, CH_2Cl_2); IR (thin film): 2996, 2987, 2982, 2969, 2938, 1811, 1724, 1666, 1465, 1368, 1343, 1306, 1271, 1183, 1105, 1044, 980 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 6.83 (dd, $J = 15.6$, 5.4 Hz, 1H), 6.18 (dd, $J = 15.6$, 1.8 Hz, 1H), 4.82 (ddd, $J = 7.2$, 5.4, 1.2 Hz, 1H), 4.31 (ddd, $J = 7.2$, 7.2, 5.4 Hz, 1H), 4.22 (q, $J = 7.2$ Hz, 2H), 1.86 (dq, $J = 15$, 7.2 Hz, 1H), 1.81 (dqd, $J = 15$, 7.2, 1.8 Hz, 1H), 1.30 (t, $J = 7.2$ Hz, 3H), 1.06 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 164.9, 153.5, 139.3, 124.8, 82.3, 79.4, 61.1, 26.3, 14.1, 8.7; CIMS calculated for $[C_{10}H_{14}O_5+Na]^+$: 237.0733. Found: 237.0735.

4.13. (*S*,*E*)-Ethyl 5-hydroxyhept-2-enoate (11b)

Following the same procedure as described for compound **11a** (see Section 4.5), **11b** was produced (135 mg, 0.76 mmol) in 84% yield from **10b** (200 mg, 0.93 mmol) as a viscous oil. Mosher ester analysis of this alcohol shows 85% ee; R_f (30% EtOAc/hexane) = 0.29; $[\alpha]_D^{25}$ 8.7 (*c* 1, CH_2Cl_2); IR (thin film): 3434, 2973,

2933, 2878, 1719, 1654, 1463, 1393, 1369, 1316, 1270, 1211, 1171, 1113, 1044, 978 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 6.95 (ddd, $J = 15.6$, 7.8, 7.2 Hz, 1H), 5.87 (dd, $J = 15.6$, 1.2 Hz, 1H), 4.15 (q, $J = 7.2$ Hz, 2H), 3.65 (dddd, $J = 7.2$, 6.6, 5.4, 4.8 Hz, 1H), 2.37 (ddd, $J = 15$, 6.6, 4.8 Hz, 1H), 2.30 (ddd, $J = 15$, 8.4, 7.8 Hz, 1H), 2.07 (br s, 1H), 1.52 (dqd, $J = 7.2$, 7.2, 4.8 Hz, 1H), 1.46 (dqd, $J = 7.8$, 7.2, 6.6 Hz, 1H), 1.25 (t, $J = 7.2$ Hz, 3H), 0.93 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.3, 145.2, 123.8, 71.8, 60.2, 39.6, 29.9, 14.2, 9.8; CIMS calculated for $[C_9H_{16}O_3+Na]^+$: 195.0992. Found: 195.1006.

4.14. (2*S*,3*R*,5*S*)-Ethyl 2,3,5-trihydroxyheptanoate (16b)

Following the same procedure as described for compound **16a** (see Section 4.7) the **16b** was produced (71 mg, 10:1 dr) in 80% yield from **11b** (75 mg, 0.44 mmol) as a viscous oil. Major isomer: R_f (100% EtOAc) = 0.29; $[\alpha]_D^{25}$ 1.3 (*c* 0.8, CH_2Cl_2); IR (thin film): 3485, 2972, 2959, 2936, 1735, 1507, 1465, 1443, 1370, 1287, 1219, 1180, 1108, 1036, 981 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.30 (q, $J = 7.8$ Hz, 1H), 4.28 (q, $J = 7.8$ Hz, 1H), 4.23 (m, 1H), 4.09 (dd, $J = 6$, 1.8 Hz, 1H), 3.88 (m, 1H), 3.23 (d, $J = 3.6$ Hz, 1H), 2.69 (d, $J = 7.8$ Hz, 1H), 2.08 (d, $J = 4.8$ Hz, 1H), 1.84–1.67 (m, 2H), 1.57–1.51 (m, 2H), 1.31 (t, $J = 7.8$ Hz, 3H), 0.96 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.2, 73.8, 70.3, 69.7, 62.1, 39.6, 30.4, 14.1, 9.9; CIMS calculated for $[C_9H_{18}O_5+Na]^+$: 229.1046. Found: 229.1049.

4.15. (3*S*,4*R*,6*S*)-6-Ethyl-tetrahydro-3,4-dihydroxypyran-2-one (21b)

Following the same procedure as described for compound **21a** (see Section 4.8), **21b** was produced (30 mg, 0.20 mmol) in 80% yield from **16b** (50 mg, 0.26 mmol) as a viscous oil. R_f (100% EtOAc) = 0.21; $[\alpha]_D^{25}$ −21.2 (*c* 0.5, CH_2Cl_2); IR (thin film): 3468, 2972, 2959, 2936, 1745, 1507, 1465, 1443, 1370, 1287, 1219, 1180, 1108, 1036, 981 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.27 (dddd, $J = 10.2$, 7.8, 6.6, 3 Hz, 1H), 4.04 (ddd, $J = 11.4$, 10.2, 3.6 Hz, 1H), 3.97 (d, $J = 10.2$ Hz, 1H), 3.35 (br s, 1H), 2.72 (br s, 1H), 2.26 (ddd, $J = 13.8$, 7.2, 3.6 Hz, 1H), 1.82 (ddd, $J = 13.2$, 11.4, 1.8 Hz, 1H), 1.81–1.68 (m, 2H), 1.01 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.0, 79.6, 74.3, 69.2, 35.2, 28.7, 9.1; CIMS calculated for $[C_7H_{11}O_4+Na_2]^+$: 205.0447. Found: 205.0445.

4.16. (2*R*,3*S*,5*S*)-Ethyl 2,3,5-trihydroxyheptanoate (17b)

Following the same procedure as described for compound **17a** (see Section 4.9), **17b** was produced (51 mg, 14:1 dr) in 86% yield from **11b** (50 mg, 0.29 mmol) as a viscous oil. Major isomer: R_f (100% EtOAc/hexane) = 0.29; $[\alpha]_D^{25}$ −4.1 (*c* 0.8, CH_2Cl_2); IR (thin film): 3459, 2971, 2931, 1738, 1507, 1448, 1374, 1301, 1261, 1214, 1140, 1079, 1028, 939 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.30 (q, $J = 7.2$ Hz, 2H), 4.21–4.17 (m, 1H), 4.06 (dd, $J = 6$, 1.8 Hz, 1H), 3.87–3.83 (m, 1H), 3.28 (br s, 1H), 3.15 (d, $J = 6$ Hz, 1H), 2.52 (br s, 1H), 1.81–1.75 (m, 2H), 1.72 (ddd, $J = 14.4$, 3, 3 Hz, 1H), 1.54 (ddd, $J = 14.4$, 7.2, 6.6 Hz, 1H), 1.32 (t, $J = 7.2$ Hz, 3H), 0.95 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.9, 73.7, 73.4, 72.9, 62.0, 39.0, 30.9, 14.1, 9.6; CIMS calculated for $[C_9H_{18}O_5+Na]^+$: 229.1046. Found: 229.1052.

4.17. (3*R*,4*S*,6*S*)-6-Ethyl-tetrahydro-3,4-dihydroxypyran-2-one (22b)

Following the same procedure as described for compound **22a** (see Section 4.10), **22b** was produced (30 mg, 0.20 mmol) in 80% yield from **17b** (50 mg, 0.26 mmol) as a viscous oil. R_f (50% EtOAc/hexane) = 0.22; $[\alpha]_D^{25}$ −5.8 (*c* 0.66, CH_2Cl_2); IR (thin film): 3468, 2972, 2959, 2936, 1745, 1507, 1465, 1443, 1370, 1287, 1219, 1180, 1108, 1036, 981 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.50 (dddd, $J = 10.8$, 7.2, 5.4, 3 Hz, 1H), 4.31 (d, $J = 7.8$ Hz, 1H), 3.99 (ddd, $J = 8.4$, 7.8, 3.6 Hz, 1H), 3.31 (br s, 1H), 2.62 (br s, 1H), 2.13 (ddd, $J = 15$, 10.8, 8.4 Hz, 1H), 1.96 (ddd, $J = 15$, 3.6, 3.6 Hz, 1H), 1.76 (ddq, $J = 14.4$, 7.8, 7.2 Hz, 1H), 1.65 (dqd, $J = 14.4$, 7.2, 6.6 Hz, 1H), 1.02 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.8, 76.9, 73.0, 69.7, 35.9, 27.9, 9.4; CIMS calculated for $[C_7H_{12}O_4+Na]^+$: 183.0627. Found: 183.0624.

4.18. (2*S*,3*R*,5*S*)-Ethyl 2,3,5-trihydroxyhexanoate (11c)

Following the same procedure as described for compound **11a** (see Section 4.5), **11c** was produced (0.22 g, 9:1 dr) in 81% yield from **10c** (0.23 g, 1.4 mmol) as a viscous oil. Major isomer: R_f (50% EtOAc/hexane) = 0.16; $[\alpha]_D^{25}$ −6 (*c* 0.4, CH_2Cl_2); IR (thin film): 3485, 2972, 2959, 2936, 1735, 1507, 1465, 1443, 1370, 1287, 1219, 1180, 1108, 1036, 981 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.29 (dd, $J = 4.2$, 1.8 Hz, 1H), 4.27 (q, $J = 7.2$ Hz, 1H), 4.22 (ddd, $J = 10.2$, 6, 3.6 Hz, 1H), 4.16 (dqd, $J = 9.6$, 6, 2.4 Hz, 1H), 4.08 (dd, $J = 6$, 2.4 Hz, 1H), 3.29 (d, $J = 6$ Hz, 1H), 2.82 (d, $J = 4.2$ Hz, 1H), 2.80 (d, $J = 6.6$ Hz, 1H), 1.88 (ddd, $J = 15$, 9.6, 3 Hz, 1H), 1.62 (ddd, $J = 15$, 8.4, 3.6 Hz, 1H), 1.31 (t, $J = 7.2$ Hz, 3H), 1.27 (d, $J = 6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.2, 73.8, 69.7, 65.1, 62.1, 41.5, 23.6, 14.1; CIMS calculated for $[C_8H_{16}O_5+Na]^+$: 215.0889. Found: 215.0892.

4.19. (3*S*,4*R*,6*S*)-Tetrahydro-3,4-dihydroxy-6-methyl-pyran-2-one (16c)

Following the same procedure as described for compound **16a** (see Section 4.7), **16c** was produced (30 mg, 0.20 mmol) in 80% yield from **11c** (50 mg, 0.26 mmol) as a viscous oil. R_f (50% EtOAc/hexane) = 0.14; $[\alpha]_D^{25}$ −2.5 (*c* 1, CH_2Cl_2); IR (thin film): 3431, 2924, 1642, 1507, 1465, 1443, 1370, 1287, 1180, 1126, 1036 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 4.47 (dqd, $J = 12$, 6, 3.6 Hz, 1H), 3.99 (dd, $J = 9.6$ Hz, 1H), 4.05 (ddd, $J = 13.8$, 9.6, 3.6 Hz, 1H), 3.41 (br s, 1H), 2.76 (br s, 1H), 2.28 (ddd, $J = 14.4$, 3.6, 3 Hz, 1H), 1.83 (ddd, $J = 13.8$, 12, 11.4 Hz, 1H), 1.44 (d, $J = 6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.1, 75.0, 74.1, 69.1, 37.5, 20.7; CIMS calculated for $[C_6H_9O_4+Na_2]^+$: 191.0291. Found: 191.0301.

4.20. (2*R*,3*S*,5*S*)-Ethyl 2,3,5-trihydroxyhexanoate (17c)

Following the same procedure as described for compound **17a** (see Section 4.9), **17c** was produced (0.23 g, 10:1 dr) in 85% yield from **11c** (0.23 g, 1.4 mmol) as a viscous oil. Major isomer: R_f (50% EtOAc/hexane) = 0.16; $[\alpha]_D^{25}$ 2.6 (*c* 1, CH_2Cl_2); IR (thin film): 3459, 2971, 2931, 1738, 1507, 1448, 1374, 1301, 1261, 1214, 1140, 1079, 1028, 939 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.31 (q, $J = 7.2$ Hz, 1H), 4.29 (q, $J = 7.2$ Hz, 1H), 4.19 (ddd, $J = 9.6$, 3, 2.4 Hz, 1H), 4.11 (dddd, $J = 15.6$, 6.6, 6, 3 Hz, 1H), 4.05 (d, $J = 2.4$ Hz, 1H), 3.14 (br s, 2H), 1.82 (ddd, $J = 14.4$, 10.2, 9.6 Hz, 1H), 1.69 (ddd, $J = 14.4$, 6, 3 Hz, 1H), 1.58 (br s, 1H), 1.32 (t, $J = 7.2$ Hz, 3H), 1.25 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.9, 73.7, 72.7, 67.8, 61.9, 41.2, 24.0, 14.1; CIMS calculated for $[C_8H_{16}O_5+Na]^+$: 215.0889. Found: 215.0892.

4.21. (3*R*,4*S*,6*S*)-Tetrahydro-3,4-dihydroxy-6-methyl-pyran-2-one (22c)

Following the same procedure as described for compound **22a** (see Section 4.10), **22c** was produced (36 mg, 0.21 mmol) in 83% yield from **17c** (50 mg, 0.26 mmol) as a viscous oil. R_f (50% EtOAc/hexane) = 0.14; $[\alpha]_D^{25}$ −32.1 (*c* 1, CH_2Cl_2); IR (thin film): 3431, 2924, 1642, 1507, 1465, 1443, 1370, 1287, 1180, 1126, 1036 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.74 (dqd, $J = 11.4$, 6, 3.6 Hz, 1H), 4.31 (d, $J = 7.8$ Hz, 1H), 4.01 (ddd, $J = 8.4$, 7.8, 3 Hz, 1H), 3.49 (br s, 1H), 2.86 (br s, 1H), 2.13 (ddd, $J = 15$, 10.8, 8.4 Hz, 1H), 1.98 (ddd, $J = 15$, 3.6, 3 Hz, 1H), 1.41 (d, $J = 6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.7, 73.1, 72.1, 69.6, 38.1, 20.7; CIMS calculated for $[C_6H_9O_4+Na_2]^+$: 191.0291. Found: 191.0301.

4.22. (*E*,4*S*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-6-(benzyloxy)-5-hydroxyhex-2-enoate (12a)

Into a 100 mL round bottomed flask fitted with a condenser and maintained under nitrogen were placed 3 g (9.8 mmol) of **10a**, 50.7 mg (0.49 mmol, 0.5 mol %) of $Pd_2(DBA)_3{\cdot}CHCl_3$, 51 mg (0.19 mmol, 2 mol %) of PPh_3, and 30 mL of CH_2Cl_2. Et_3N (1.3 mL, 9.8 mmol) and *p*-methoxyphenol (2.43 g, 19.6 mmol) were added and the mixture was heated at reflux for 30 min. The reaction was cooled to rt and quenched by the addition of saturated aqueous sodium bicarbonate (20 mL). The aqueous layer was extracted with ether (3 × 30 mL). The organic layer was washed with brine (20 mL) and dried with anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (7:3, hexanes/EtOAc) afforded **12a** as a yellow oil (3.4 g, 90%). Mosher ester analysis of this alcohol shows 90% ee; R_f (30% EtOAc/hexanes) = 0.32; $[\alpha]_D^{25}$ 22.5 (*c* 1.1, CH_2Cl_2); IR (thin film): 3484, 2980, 2954, 2923, 2869, 1716, 1660, 1506, 1454, 1368, 1303, 1276, 1227, 1180, 1109, 1036, 983 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.33 (m, 5H), 6.98 (dd, $J = 15.6$, 5.4 Hz, 1H), 6.81 (m, 4H), 6.07 (dd, $J = 15.6$, 1.8 Hz, 1H), 4.86 (ddd, $J = 5.4$, 4.8, 1.8 Hz, 1H), 4.56 (d, $J = 12$ Hz, 1H), 4.53 (d, $J = 12$ Hz, 1H), 4.18 (q, $J = 7.8$ Hz, 1H), 4.16 (q, $J = 7.8$ Hz, 1H), 4.01 (ddd, $J = 10.2$, 6, 5.4 Hz, 1H), 3.76 (s, 3H), 3.68 (dd, $J = 9.6$, 4.8 Hz, 1H), 3.60 (dd, $J = 9.6$, 5.4 Hz, 1H), 2.58 (d, $J = 5.4$ Hz, 1H), 1.27 (t, $J = 7.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 165.7, 154.5, 151.6, 143.5, 137.6, 128.4 (2C), 127.8 (3C), 123.8, 117.0 (2C), 114.6 (2C), 78.4, 73.6, 72.3, 69.9, 60.6, 55.6, 14.1; CIMS calculated for $[C_{22}H_{26}O_6+Na]^+$: 409.1627. Found: 409.1621.

4.23. (2*S*,3*S*,4*R*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-6-(benzyloxy)-2,3,5-trihydroxyhexanoate (18a)

Into a 25 mL round bottomed flask was added **12a** (193 mg, 0.5 mmol) and followed by 1 mL of *t*-BuOH, 1 mL of acetone and then the solution was cooled to 0 °C. To this solution 0.35 mL of 50% NMO in H_2O (1.5 mmol) and OsO_4 (2.5 mg, 0.01 mmol, 2 mol %) were added, and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (100 mg) at rt. Then the mixture was filtered through a pad of Celite/Florisil and eluted with 20 mL of 50% EtOAc/CH_3OH. The combined organic layers were dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (6:4, hexanes/EtOAc) afforded **18a** (172 mg, 7:1 dr, 82% yield) as a viscous oil. Major isomer: R_f (90% EtOAc/hexanes) = 0.43; $[\alpha]_D^{25}$ 5.4 (*c* 1.0, CH_2Cl_2); IR (thin film): 3533, 2983, 2957, 2869, 1747, 1653, 1593, 1506, 1466, 1455, 1372, 1296, 1220, 1184,

1044 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.28 (m, 5H), 6.98 (m, 2H), 6.80 (m, 2H), 4.49 (dd, $J = 9$, 1.8 Hz, 1H), 4.46 (d, $J = 11.4$ Hz, 1H), 4.43 (d, $J = 11.4$ Hz, 1H), 4.35–4.29 (m, 3H), 3.76 (s, 3H), 4.28 (q, $J = 7.2$ Hz, 1H), 4.26 (q, $J = 7.2$ Hz, 1H), 3.67 (dd, $J = 9.6$, 6 Hz, 1H), 3.55 (dd, $J = 9.6$, 6 Hz, 1H), 3.18 (d, $J = 5.4$ Hz, 1H), 2.89 (d, $J = 8.4$ Hz, 1H), 2.62 (d, $J = 7.8$ Hz, 1H), 1.29 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 173.4, 154.4, 152.4, 137.5, 128.4 (2C), 127.8 (3C), 117.1 (2C), 114.7 (2C), 76.6, 73.4, 71.1, 70.6, 70.1, 69.3, 62.1, 55.6, 14.1; CIMS calculated for $[C_{22}H_{28}O_8+Na]^+$: 443.1682. Found: 443.1668.

4.24. (2*S*,3*S*,4*R*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-6-(benzyloxy)-2,3,5-trihydroxyhexanoate (18a)

Into a 50 mL round bottomed flask were added 10 mL of *t*-BuOH, 10 mL of water, $K_3Fe(CN)_6$ (4.93 g, 15 mmol), K_2CO_3 (2.07 g, 15 mmol), $MeSO_2NH_2$ (475 mg, 5 mmol), $(DHQD)_2PHAL$ (85 mg, 0.1 mmol, 2.1 mol %), and OsO_4 (25 mg, 0.1 mmol, 2 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added **12a** (2.00 g, 5 mmol) in 4 mL CH_2Cl_2, and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (100 mg) at rt and stirred for 15 min. Then the mixture was filtered through a pad of Celite/Florisil and eluted with 50 mL of 50% EtOAc/CH_3OH. The combined organic layers were dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (6:4, hexanes/EtOAc) afforded 1.8 g (86% yield) of **18a** as a viscous oil (25:1 dr). R_f (90% EtOAc/hexanes) = 0.43; $[\alpha]_D^{25}$ 5.4 (*c* 1.0, CH_2Cl_2); for the remaining spectral data see Experimental 4.23.

4.25. (3*S*,4*S*,5*S*,6*S*)-5-(4-Methoxyphenoxy)-6-((benzyloxy)methyl)-tetrahydro-3,4-dihydroxypyran-2-one (23a)

To a solution of **18a** (200 mg, 0.48 mmol) in benzene (3 mL) was added pyridinium toluenesulfonate (6 mg, 0.03 mmol, 5 mol %) and the mixture was heated at reflux for 5 h. The reaction was cooled to rt and quenched by the addition of saturated aqueous sodium bicarbonate (2 mL). The aqueous layer was extracted with ether (3 × 10 mL). The organic layer was washed with brine (10 mL) and dried with anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (4:6, hexanes/EtOAc) afforded **23a** as a viscous oil (160 mg, 85%): R_f (90% EtOAc/hexanes) = 0.40; $[\alpha]_D^{25}$ −26.8 (*c* 2, CH_2Cl_2); IR (thin film): 3396, 2929, 2922, 1740, 1506, 1455, 1368, 1328, 1220, 1103, 1034, 923, 830 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.26 (m, 3H), 7.03 (m, 4H), 6.78 (m, 2H), 4.8 (dd, $J = 2.4$, 1.8 Hz, 1H), 4.59 (d, $J = 10.2$ Hz, 1H), 4.54 (ddd, $J = 7.2$, 6.6, 1.8 Hz, 1H), 4.36 (d, $J = 11.4$ Hz, 1H), 4.28 (d, $J = 11.4$ Hz, 1H), 4.17 (ddd, $J = 10.2$, 1.8, 1.2 Hz, 1H), 3.81 (br s, 1H), 3.74 (s, 3H), 3.72 (d, $J = 6.6$ Hz, 2H), 3.21 (br s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.1, 154.8, 153.5, 137.0, 128.4 (2C), 127.9 (2C), 127.8, 117.7 (2C), 114.6 (2C), 78.2, 76.7, 73.5, 71.8, 70.4, 67.0, 55.7; CIMS calculated for $[C_{20}H_{22}O_7+Na]^+$: 397.1257. Found: 397.1285.

4.26. (3*S*,4*R*,5*R*,6*S*)-5-(4-Methoxyphenoxy)-6-((benzyloxy)methyl)-tetrahydro-3,4-diacetoxypyran-2-one (24a)

To a solution of **23a** (150 mg, 0.4 mmol) in CH_2Cl_2 (2 mL) were added excess Ac_2O (0.6 mL, 2 mmol), pyridine (0.3 mL, 4 mmol) and a catalytic amount of DMAP (2.5 mg, 5 mol %). The reaction was stirred for 1 h, after which 10 mL ether and 10 mL of saturated NH_4Cl were added to remove excess base. The organic layer was washed with 10 mL $CuSO_4$ solution, 10 mL brine and the aqueous layer was further extracted with ether (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed in vacuo. The crude product was purified by flash chromatography on silica gel (4:1, hexanes/EtOAc) to yield **24a** (174 mg, 95% yield) as a viscous oil. R_f (40% EtOAc/hexanes) = 0.38; $[\alpha]_D^{25}$ −59.7 (*c* 1.0, CH_2Cl_2); IR (thin film): 2953, 2922, 2876, 2863, 1754, 1507, 1455, 1373, 1209, 1087, 1034, 929 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 7.29 (m, 3H), 7.19 (m, 2H), 6.94 (m, 2H), 6.79 (m, 2H), 5.49 (d, $J = 10.2$ Hz, 1H), 5.41 (dd, $J = 10.2$, 2.4 Hz, 1H), 5.04 (dd, $J = 2.4$, 1.4 Hz, 1H), 4.73 (ddd, $J = 7.3$, 7.1, 1.4 Hz, 1H), 4.46 (d, $J = 11.4$ Hz, 1H), 4.38 (d, $J = 11.4$ Hz, 1H), 3.78 (d, $J = 7.1$ Hz, 2H), 3.77 (s, 3H), 2.15 (s, 3H), 1.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 170.2, 170.1, 165.7, 154.9, 152.9, 136.9, 128.4 (2C), 128.0, 127.9 (2C), 117.7 (2C), 114.6 (2C), 76.5, 73.6, 73.2, 71.4, 69.4, 66.3, 55.6, 20.5, 20.4; CIMS calculated for $[C_{24}H_{26}O_9+Na]^+$: 481.1475. Found: 481.1466.

4.27. (*E*,4*S*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-5-hydroxyhept-2-enoate (12b)

Following the same procedure as described for compound **12c** (see Section 4.32), **12b** was produced (1.23 g, 4.1 mmol) in 90% yield from **10b** (1 g, 4.6 mmol) as a viscous oil. Mosher ester analysis of this alcohol shows 85% ee; R_f (20% EtOAc/hexane) = 0.22; $[\alpha]_D^{25}$ 37.8 (*c* 1, CH_2Cl_2); IR (thin film): 3485, 2977, 2963, 2936, 2903, 2878, 1717, 1658, 1508, 1465, 1443, 1393, 1369, 1302, 1225, 1180, 1037, 980 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 6.95 (dd, $J = 15.6$, 6 Hz, 1H), 6.83 (m, 2H), 6.79 (m, 2H), 6.04 (dd, $J = 15.6$, 1.8 Hz, 1H), 4.52 (ddd, $J = 6$, 6, 1.2 Hz, 1H), 4.18 (q, $J = 7.2$ Hz, 1H), 4.16 (q, $J = 7.2$ Hz, 1H), 3.75 (s, 3H), 3.69 (dddd, $J = 7.2$, 6, 5.4, 4.8 Hz, 1H), 2.48 (d, $J = 4.8$ Hz, 1H), 1.67 (dqd, $J = 15$, 7.2, 4.2 Hz, 1H),

1.55 (dqd, $J = 15$, 7.2, 4.8 Hz, 1H), 1.27 (t, $J = 7.2$ Hz, 3H), 1.02 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 165.7, 154.5, 151.6, 143.8, 124.1, 117.1 (2C), 114.6 (2C), 81.5, 74.7, 60.6, 55.6, 25.6, 14.1, 9.8; CIMS calculated for $[C_{16}H_{22}O_5+Na]^+$: 317.1359. Found: 317.1344.

4.28. (2*S*,3*S*,4*R*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-2,3,5-trihydroxyheptanoate (18b)

Following the same procedure as described for compound **18a** (see Section 4.23), **18b** was produced (89 mg, 0.27 mmol) in 80% yield from **12b** (100 mg, 0.34 mmol) as a viscous oil (6:1 dr). Major isomer: R_f (50% EtOAc/hexane) = 0.30; $[\alpha]_D^{25}$ −3.1 (*c* 2, CH_2Cl_2); IR (thin film): 3485, 2963, 2936, 2905, 2876, 1736, 1508, 1464, 1442, 1393, 1370, 1288, 1227, 1182, 1110, 1037, 981 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.98 (m, 2H), 6.81 (m, 2H), 4.35 (d, $J = 5.4$ Hz, 1H), 4.32–4.29 (m, 2H), 4.27 (q, $J = 7.2$ Hz, 2H), 3.91 (ddd, $J = 8.4$, 7.2, 6 Hz, 1H), 3.75 (s, 3H), 3.30 (d, $J = 6$ Hz, 1H), 2.97 (d, $J = 4.2$ Hz, 1H), 2.23 (d, $J = 4.8$ Hz, 1H), 1.59 (dqd, $J = 15$, 7.2, 3.6 Hz, 1H), 1.57 (dqd, $J = 15$, 7.2, 4.8 Hz, 1H), 1.30 (t, $J = 7.2$ Hz, 3H), 0.95 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.5, 154.4, 152.6, 117.1 (2C), 114.7 (2C), 78.7, 72.5, 71.2, 70.2, 62.2, 55.6, 26.7, 14.1, 10.4; CIMS calculated for $[C_{16}H_{24}O_7+Na]^+$: 351.1414. Found: 351.1429.

4.29. (2*S*,3*S*,4*R*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-2,3,5-trihydroxyheptanoate (18b)

Following the same procedure as described for compound **18a** (see Section 4.24), **18b** was produced (0.47 g, 1.4 mmol) in 85% yield from **12b** (0.5 g, 1.7 mmol) as a viscous oil (20:1 dr). R_f (50% EtOAc/hexane) = 0.30; $[\alpha]_D^{25}$ −3.1 (*c* 2, CH_2Cl_2); for the remaining spectral data see Experimental 4.28.

4.30. (3*S*,4*S*,5*S*,6*S*)-5-(4-Methoxyphenoxy)-6-ethyltetrahydro-3,4-dihydroxypyran-2-one (23b)

Following the same procedure as described for compound **23a** (see Section 4.25), **23b** was produced (220 mg, 0.77 mmol) in 86% yield from **18b** (300 mg, 0.9 mmol) as a viscous oil. R_f (50% EtOAc/hexane) = 0.28; $[\alpha]_D^{25}$ −47.4 (*c* 2.2, CH_2Cl_2); IR (thin film): 3438, 2970, 2938, 2926, 1740, 1506, 1464, 1442, 1370, 1290, 1224, 1141, 1106, 1035, 876 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.06 (m, 2H), 6.82 (m, 2H), 4.63 (dd, $J = 2.4$, 1.8 Hz, 1H), 4.57 (d, $J = 10.8$ Hz, 1H), 4.29 (ddd, $J = 7.8$, 6, 1.8 Hz, 1H), 4.18 (ddd, $J = 10.8$, 3.6, 2.4 Hz, 1H), 3.77 (s, 3H), 3.22 (d, $J = 5.4$ Hz, 1H), 2.67 (d, $J = 4.8$ Hz, 1H), 1.97 (dq, $J = 19.2$, 7.8 Hz, 1H), 1.74 (dq, $J = 19.2$, 7.8 Hz, 1H), 0.93 (t, $J = 7.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.8, 154.6, 153.7, 117.7 (2C), 114.6 (2C), 82.1, 77.9, 71.8, 70.1, 55.6, 24.2, 9.6; CIMS calculated for $[C_{14}H_{18}O_6+Na]^+$: 305.0995. Found: 305.0971.

4.31. (3*S*,4*S*,5*S*,6*S*)-5-(4-Methoxyphenoxy)-6-ethyltetrahydro-3,4-diacetoxypyran-2-one (24b)

Following the same procedure as described for compound **24a** (see Section 4.26), **24b** was produced (0.12 g, 0.32 mmol) in 94% yield from **23b** (100 mg, 0.35 mmol) as a viscous oil. R_f (50% EtOAc/hexane) = 0.58; $[\alpha]_D^{25}$ 56.5 (*c* 0.4, CH_2Cl_2); IR (thin film): 1748, 1507, 1443, 1374, 1209, 1085, 1033, 795 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 6.88 (m, 2H), 6.82 (m, 2H), 5.47 (d, $J = 10.2$ Hz, 1H), 5.41 (dd, $J = 10.2$, 2.4 Hz, 1H), 4.81 (dd, $J = 2.4$, 1.2 Hz, 1H), 4.45 (ddd, $J = 7.2$, 6.6, 1.2 Hz, 1H), 3.74 (s, 3H), 2.16 (s, 3H), 1.86 (s, 3H), 1.98 (dqd, $J = 15$, 7.8, 7,2 Hz, 1H), 1.75 (dqd, $J = 15$, 7.8, 4.8 Hz, 1H), 1.01 (t, $J = 7.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.4, 170.1, 166.1, 154.9, 152.8, 117.4 (2C), 114.8 (2C), 80.5, 74.8, 72.0, 69.1, 55.7, 23.2, 20.5 (2C), 9.6; CIMS calculated for $[C_{18}H_{22}O_8+Na]^+$: 389.1206. Found: 389.1224.

4.32. (*E*,4*S*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-5-hydroxyhex-2-enoate (12c)

Into a 50 mL round bottomed flask fitted with a condenser and maintained under nitrogen was placed 1 g (5 mmol) of **10c**, 26 mg (0.025 mmol, 0.5 mol %) of $Pd_2(DBA)_3{\cdot}CHCl_3$, 26.2 mg (0.1 mmol, 2 mol %) of PPh_3, and 10 mL of CH_2Cl_2. Et_3N (0.7 mL, 5 mmol) and *p*-methoxyphenol (3.1 g, 25 mmol) were added and the mixture was allowed to stirr at rt for 12 h. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate (10 mL). The aqueous layer was extracted with ether (3 × 20 mL). The organic layer was washed with brine (10 mL) and dried with anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (6:1, hexanes/EtOAc) afforded **12c** as a yellow oil (1.19 g, 85%). Mosher ester analysis of this alcohol shows 80% ee; R_f (40% EtOAc/hexanes) = 0.37; $[\alpha]_D^{25}$ 46.9 (*c* 2, CH_2Cl_2); IR (thin film): 3484, 2980, 2933, 2905, 2890, 1717, 1659, 1511, 1466, 1369, 1276, 1225, 1179, 1093, 1036, 984 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 6.92 (dd, $J = 15.6$, 6 Hz, 1H), 6.81 (m, 2H), 6.78 (m, 2H), 6.04 (dd, $J = 15.6$, 1.8 Hz, 1H), 4.44 (ddd, $J = 6.6$, 6, 1.2 Hz, 1H), 4.16 (q, $J = 7.2$ Hz, 1H), 4.14 (q, $J = 7.2$ Hz, 1H), 3.92 (qd, $J = 6.6$, 3.6 Hz, 1H), 3.73 (s, 3H), 2.79 (d, $J = 3.6$ Hz, 1H), 1.26 (d, $J = 6.6$ Hz, 3H), 1.25 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 165.6, 154.5, 151.5, 143.5, 124.1, 117.1 (2C), 114.6 (2C), 83.0, 69.5, 60.5, 55.5, 18.3, 14.1; CIMS calculated for $[C_{15}H_{20}O_5+Na]^+$: 303.1203. Found: 303.1219.

4.33. (2*S*,3*S*,4*R*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-2,3,5-trihydroxyhexanoate (18c)

Following the same procedure as described for compound **18a** (see Section 4.23), **18c** was produced (86 mg, 0.27 mmol) in 77% yield from **12c** (100 mg, 0.36 mmol) as a viscous oil (6:1 dr). Major isomer: R_f (100% EtOAc) = 0.50; $[\alpha]_D^{25}$ 5.1 (*c* 1, CH_2Cl_2); IR (thin film): 3433, 2980, 2976, 2933, 2906, 1735, 1507, 1443, 1371, 1327, 1291, 1220, 1153, 1112, 1045, 992, 828 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 6.97 (m, 2H), 6.80 (m, 2H), 4.35 (d, $J = 6$ Hz, 1H), 4.30–4.21 (m, 3H), 4.28 (q, $J = 7.2$ Hz, 1H), 4.26 (q, $J = 7.2$ Hz, 1H), 3.74 (s, 3H), 3.47 (d, $J = 6$ Hz, 1H), 3.44 (d, $J = 6.6$ Hz, 1H), 2.70 (d, $J = 7.8$ Hz, 1H), 1.29 (t, $J = 7.2$ Hz, 3H), 1.27 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 173.5, 154.3, 152.6, 117.0 (2C), 114.7 (2C), 79.1, 71.3, 70.3, 66.9, 62.1, 55.6, 19.2, 14.1; CIMS calculated for $[C_{15}H_{22}O_7+Na]^+$: 337.1257. Found: 337.1285.

4.34. (2*S*,3*S*,4*R*,5*S*)-Ethyl 4-(4-methoxyphenoxy)-2,3,5-trihydroxyhexanoate (18c)

Following the same procedure as described for compound **18a** (see Section 4.24), **18c** was produced (280 mg, 0.89 mmol) in 83% yield from **12c** (300 mg, 1.07 mmol) as a viscous oil (20:1 dr). R_f (100% EtOAc) = 0.50; $[\alpha]_D^{25}$ 5.1 (*c* 1, CH_2Cl_2); For the remaining spectral data see Section 4.33.

4.35. (3*S*,4*S*,5*S*,6*S*)-5-(4-methoxyphenoxy)-tetrahydro-3,4-dihydroxy-6-methylpyran-2-one (23c)

Following the same procedure as described for compound **23a** (see Section 4.25), **23c** was produced (66 mg, 0.25 mmol) in 80% yield from **18c** (100 mg, 0.31 mmol) as a viscous oil. R_f (70% EtOAc/hexane) = 0.16; $[\alpha]_D^{25}$ −84.3 (*c* 1, CH_2Cl_2); IR (thin film): 3416, 2980, 2976, 2933, 1733, 1507, 1443, 1326, 1222, 1155, 1106, 1033, 829 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.03 (m, 2H), 6.81 (m, 2H), 4.56 (d, $J = 10.2$ Hz, 1H), 4.54 (qd, $J = 6.6$, 1.8 Hz, 1H), 4.46 (dd, $J = 2.4$, 1.8 Hz, 1H), 4.20 (dd, $J = 10.2$, 2.4 Hz, 1H), 4.10 (br s, 1H), 3.75 (s, 3H), 3.55 (br s, 1H), 1.39 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.8, 154.8, 153.7, 117.8 (2C), 114.6 (2C), 79.2, 76.9, 71.9, 69.8, 55.6, 17.0; CIMS: Calculated for $[C_{13}H_{16}O_6+Na]^+$: 291.0839. Found: 291.0832.

4.36. (3*S*,4*R*,5*R*,6*S*)-5-(4-Methoxyphenoxy)-tetrahydro-3,4-diacetoxy-6-methylpyran-2-one (24c)

Following the same procedure as described for compound **24a** (see Section 4.26), **24c** was produced (59 mg, 0.16 mmol) in 90% yield from **23c** (50 mg, 0.18 mmol) as a viscous oil. R_f (70% EtOAc/hexane) = 0.76; $[\alpha]_D^{25}$ −85.6 (*c* 0.3, CH_2Cl_2); IR (thin film): 1748, 1507, 1443, 1374, 1209, 1085, 1033, 795 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 6.88 (m, 2H), 6.82 (m, 2H), 5.48 (d, $J = 10.2$ Hz, 1H), 5.41 (dd, $J = 10.2$, 2.4 Hz, 1H), 4.75 (qd, $J = 6.6$, 1.2 Hz, 1H), 4.72 (dd, $J = 2.4$, 1.2 Hz, 1H), 3.77 (s, 3H), 2.16 (s, 3H), 1.86 (s, 3H), 1.49 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.4, 170.3, 166.2, 154.6, 152.9, 117.6 (2C), 114.7 (2C), 89.2, 76.4, 75.3, 72.1, 55.6, 20.5 (2C), 17.1; CIMS calculated for $[C_{17}H_{20}O_8+Na]^+$: 375.1050. Found: 375.1040.

4.37. (*E*,2*S*,3*R*)-5-(Ethoxycarbonyl)-1-(benzyloxy)-3-fluoropent-4-en-2-yl 3-methylbenzoate (14a)

Into a 10 mL round bottomed Teflon PFA tube were added **2a** (1.3 g, 4.6 mmol), *N*,*N*-diethyl-α,α-difluoro-(*meta*-methylbenzyl)amine (DFMBA, 1.98 g, 9.3 mmol), and heptane (2 mL). The mixture was stirred at 98 °C for about 2 h. After completion of the reaction, the mixture was poured into aqueous $NaHCO_3$ and extracted with ether (3 × 25 mL). The combined organic layers were dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (1:9, EtOAc/hexanes) afforded 1.3 g of **14a** as a viscous oil (70% yield, 90% ee). R_f (40% EtOAc/hexane) = 0.58; $[\alpha]_D^{25}$ 19.5 (*c* 1.5, CH_2Cl_2); IR (thin film): 2981, 2924, 2872, 1718, 1665, 1590, 1454, 1367, 1300, 1270, 1194, 1180, 1100, 1037, 976 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.84 (m, 2H), 7.33 (m, 7H), 7.01 (ddd, $J = 20.4$, 15.6, 4.8 Hz, 1H), 6.17 (ddd, $J = 15.6$, 1.8, 1.8 Hz, 1H), 5.47 (dddd, $J = 48$, 4.8, 4.2, 1.8 Hz, 1H), 5.45 (ddd, $J = 20.4$, 9.6, 1.8 Hz, 1H), 4.58 (d, $J = 12$ Hz, 1H), 4.54 (d, $J = 12$ Hz, 1H), 4.22 (q, $J = 7.2$ Hz, 2H), 3.82 (ddd, $J = 10.8$, 6, 1.8 Hz, 1H), 3.75 (dd, $J = 10.8$, 4.8 Hz, 1H), 2.41 (s, 3H), 1.29 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 165.7, 165.4, 140.3 (d, $J = 18.5$ Hz), 138.2, 137.5, 134.1, 130.3, 129.3, 128.4 (2C), 128.3, 127.8 (2C), 127.6, 126.9, 123.6 (d, $J = 11.1$ Hz), 90.1 (d, $J = 177.7$ Hz), 73.4, 72.9 (d, $J = 23.1$ Hz), 66.9 (d, $J = 6.5$ Hz), 60.7, 21.2, 14.1; CIMS calculated for $[C_{23}H_{25}FO_5+Na]^+$: 423.1578. Found: 423.1579.

4.38. (*E*,4*R*,5*S*)-Ethyl 6-(benzyloxy)-4-fluoro-5-hydroxyhex-2-enoate (15a)

To a solution of **14a** (500 mg, 1.25 mmol) in EtOH (3 mL) was added 10% HCl in EtOH (0.5 mL), and the mixture was heated at reflux for 24 h. Then EtOH was removed under reduced pressure, flash chromatography on silica gel (8:2, hexanes/EtOAc) afforded **15a** as a viscous oil (211 mg, 60%). Mosher ester analysis

of this alcohol showed 90% ee; R_f (40% EtOAc/hexane) = 0.36; $[\alpha]_D^{25}$ 24.6 (*c* 2.2, CH_2Cl_2); IR (thin film): 3435, 2981, 2924, 2872, 1718, 1590, 1454, 1367, 1300, 1270, 1194, 1180, 1100, 1037, 976 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.35 (m, 5H), 7.02 (ddd, $J = 21.6$, 15.6, 4.2 Hz, 1H), 6.14 (ddd, $J = 15.6$, 1.8, 1.8 Hz, 1H), 5.12 (dddd, $J = 46.8$, 6.6, 4.2, 1.8 Hz, 1H), 4.57 (br s, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 3.93 (ddd, $J = 21.6$, 6.6, 4.8 Hz, 1H), 3.64 (dd, $J = 4.8$, 1.8 Hz, 1H), 3.63 (dd, $J = 4.8$, 1.8 Hz, 1H), 2.50 (d, $J = 6$ Hz, 1H), 2.49 (s, 3H), 1.30 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 165.7, 141.6 (d, $J = 17.2$ Hz), 137.4, 128.5 (2C), 127.9, 127.8 (2C), 122.9 (d, $J = 11.6$ Hz), 91.1 (d, $J = 176.5$ Hz), 73.6, 71.4 (d, $J = 23.9$ Hz), 69.5 (d, $J = 4.5$ Hz), 60.7, 21.2, 14.1; CIMS calculated for $[C_{15}H_{19}FO_4+Na]^+$: 305.1159. Found: 305.1161.

4.39. (2*R*,3*R*,4*S*,5*S*)-Ethyl 6-(benzyloxy)-4-fluoro-2,3,5-trihydroxyhexanoate (19a)

Into a 50 mL round bottomed flask were added 3 mL of *t*-BuOH, 3 mL of water, $K_3Fe(CN)_6$ (350 mg, 1.06 mmol), K_2CO_3 (147 mg, 1.06 mmol), $MeSO_2NH_2$ (34 mg, 0.35 mmol), $(DHQ)_2PHAL$ (5.8 mg, 7.4 μmol, 2.1 mol %), and OsO_4 (1.8 mg, 7.0 μmol, 2 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added **15a** (100 mg, 0.35 mmol) and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (50 mg) at rt. EtOAc (10 mL) was added to the reaction mixture and after separation of the layers, the aqueous phase was further extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (1:1, hexanes/EtOAc) afforded **19a** as a viscous oil (96 mg, 86%, 7:1 dr). Major isomer: R_f (40% EtOAc/hexane) = 0.15; $[\alpha]_D^{25}$ −2.1 (*c* 2.7, CH_2Cl_2); IR (thin film): 3402, 3033, 2922, 2862, 1736, 1496, 1453, 1365, 1216, 1072, 1026, 811 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.33 (m, 5H), 4.60 (ddd, $J = 46.6$, 8.4, 6.6 Hz, 1H), 4.58 (br s, 2H), 4.39 (dd, $J = 6.6$, 1.2 Hz, 1H), 4.29 (q, $J = 7.2$ Hz, 2H), 4.22 (ddd, $J = 13.2$, 6.6, 1.2 Hz, 1H), 4.14 (dddd, $J = 16.2$, 6.6, 6, 5.4 Hz, 1H), 3.72 (dd, $J = 9.6$, 6 Hz, 1H), 3.66 (dd, $J = 9.6$, 6.6 Hz, 1H), 3.49 (d, $J = 5.4$ Hz, 1H), 3.33 (d, $J = 6.6$ Hz, 1H), 3.09 (d, $J = 4.8$ Hz, 1H), 1.30 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.8, 137.3, 128.5 (2C), 128.0, 127.8 (2C), 89.1 (d, $J = 175.4$ Hz), 73.7, 71.8 (d, $J = 25.5$ Hz), 71.2 (d, $J = 24.7$ Hz), 70.0 (d, $J = 3.5$ Hz), 69.9 (d, $J = 5.8$ Hz), 62.1, 14.1; CIMS calculated for $[C_{15}H_{21}FO_6+Na]^+$: 339.1214. Found: 339.1217.

4.40. (2*R*,3*R*,4*S*,5*S*)-Ethyl 6-(benzyloxy)-4-fluoro-2,3,5-trihydroxyhexanoate (19a)

To a solution of **15a** (100 mg, 0.35 mmol) in 0.5 mL of *t*-BuOH/0.5 mL of acetone were added 0.25 mL of 50% NMO in H_2O (125 mg, 1.06 mmol) and 1.8 mg OsO_4 (0.007 mmol, 2 mol %). The reaction mixture was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (50 mg) at rt and filtered through a pad of Celite and eluted with CH_3OH and dried over sodium sulfate. Then the solvent was removed under reduced pressure and flash chromatography on silica gel (1:1, hexanes/EtOAc) afforded **19a** as a viscous oil (101 mg, 90%, 5:1 dr). Major isomer: R_f (40% EtOAc/hexane) = 0.15; $[\alpha]_D^{25}$ −2.1 (*c* 2.7, CH_2Cl_2); For the remaining spectral data see Section 4.39.

4.41. (2*S*,3*S*,4*S*,5*S*)-Ethyl 6-(benzyloxy)-4-fluoro-2,3,5-trihydroxyhexanoate (20a)

Into a 50 mL round bottomed flask were added 3 mL of *t*-BuOH, 3 mL of water, $K_3Fe(CN)_6$ (350 mg, 1.06 mmol), K_2CO_3 (147 mg, 1.06 mmol), $MeSO_2NH_2$ (34 mg, 0.35 mmol), $(DHQD)_2PHAL$ (5.8 mg, 7.4 μmol, 2.1 mol %), and OsO_4 (1.8 mg, 7.0 μmol, 2 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added **15a** (100 mg, 0.35 mmol) and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (50 mg) at rt. EtOAc (10 mL) was added to the reaction mixture and after separation of the layers, the aqueous phase was further extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (1:1, hexanes/EtOAc) afforded **20a** as a viscous oil (95 mg, 85%, 2:1 dr). Major isomer: R_f (40% EtOAc/hexane) = 0.14; $[\alpha]_D^{25}$ −3.2 (*c* 1.0, CH_2Cl_2); IR (thin film): 3402, 3033, 2922, 2862, 1736, 1496, 1453, 1365, 1216, 1072, 1026, 811 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.33 (m, 5H), 4.64 (ddd, $J = 46.2$, 7.8, 3 Hz, 1H), 4.55 (br s, 2H), 4.38 (d, $J = 3$ Hz, 1H), 4.26 (q, $J = 7.2$ Hz, 2H), 4.22 (ddd, $J = 12.5$, 3.6, 2.4 Hz, 1H), 4.12 (dddd, $J = 12$, 6.6, 5.4, 2.4 Hz, 1H), 3.69 (dd, $J = 9.6$, 6 Hz, 1H), 3.63 (dd, $J = 9.6$, 5.4 Hz, 1H), 3.30 (d, $J = 4.2$ Hz, 1H), 2.08 (d, $J = 9$ Hz, 1H), 2.88 (d, $J = 6.6$ Hz, 1H), 1.28 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.8, 137.3, 128.5 (2C), 128.0, 127.8 (2C), 89.1 (d, $J = 175.4$ Hz), 73.7, 71.8 (d, $J = 25.5$ Hz), 71.2 (d, $J = 24.7$ Hz), 70.0 (d, $J = 3.5$ Hz), 69.9 (d, $J = 5.8$ Hz), 62.1, 14.1; CIMS calculated for $[C_{15}H_{21}FO_6+Na]^+$: 339.1214. Found: 339.1217.

4.42. (2*S*,3*R*,4*R*,5*R*)-5-(Ethoxycarbonyl)-1-(benzyloxy)-3-fluoro-4,5-dihydroxypentan-2-yl 3-methylbenzoate (27a)

Into a 50 mL round bottomed flask were added 4 mL of *t*-BuOH, 4 mL of water, $K_3Fe(CN)_6$ (370 mg, 1.13 mmol), K_2CO_3 (155 mg, 1.13 mmol), $MeSO_2NH_2$ (36 mg, 0.38 mmol), $(DHQ)_2PHAL$ (6.1 mg, 7.9 μmol, 2.1 mol %), and OsO_4 (1.9 mg, 7.5 μmol, 2 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added **14a** (150 mg, 0.38 mmol) and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (50 mg) at rt. EtOAc (15 mL) was added to the reaction mixture and after separation of the layers, the aqueous phase was further extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (3:1, hexanes/EtOAc) afforded **27a** as a viscous oil (130 mg, 80%, 6:1 dr). Major isomer: R_f (50% EtOAc/hexane) = 0.43; $[\alpha]_D^{25}$ −4.13 (*c* 2.3, CH_2Cl_2); IR (thin film): 3455, 3032, 2924, 1720, 1608, 1590, 1454, 1369, 1273, 1196, 1099, 1078, 1022, 930, 864 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.87 (m, 2H), 7.30 (m, 7H), 5.73 (dddd, *J* = 24, 6.6, 4.2, 2.4 Hz, 1H), 4.91 (ddd, *J* = 46.2, 8.4, 2.4 Hz, 1H), 4.60 (br s, 2H), 4.43 (d, *J* = 6, 1H), 4.34 (ddd, *J* = 8.4, 8.4, 6, 1H), 4.29 (qd, *J* = 7.2, 1.8 Hz, 1H), 4.28 (qd, *J* = 7.2, 1.8 Hz, 1H), 3.98 (dd, *J* = 10.8, 6 Hz, 1H), 3.81 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.31 (d, *J* = 8.4 Hz, 1H), 3.29 (d, *J* = 6 Hz, 1H), 2.40 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.8, 165.8, 138.2, 137.1, 134.1, 130.3, 129.5, 128.4 (2C), 128.3, 127.9, 127.7 (2C), 126.9, 91.1 (d, *J* = 179.4 Hz), 73.5, 71.6 (d, *J* = 20.1 Hz), 70.0 (d, *J* = 25.9 Hz), 69.9 (d, *J* = 2.2 Hz), 66.8 (d, *J* = 8.1 Hz), 62.2, 21.2, 14.1; CIMS calculated for $[C_{15}H_{27}FO_7+Na]^+$: 457.1633. Found: 457.1635.

4.43. (2*S*,3*R*,4*R*,5*R*)-5-(Ethoxycarbonyl)-1-(benzyloxy)-3-fluoro-4,5-dihydroxypentan-2-yl 3-methylbenzoate (27a)

To a solution of **14a** (100 mg, 0.25 mmol) in 0.5 mL of *t*-BuOH/0.5 mL of acetone were added 0.18 mL of 50% NMO in H_2O (88 mg, 0.75 mmol) and 1.8 mg OsO_4 (5.0 μmol, 2 mol %). The reaction mixture was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (50 mg) at rt and filtered through a pad of Celite and eluted with CH_3OH and dried over sodium sulfate. Then the solvent was removed under reduced pressure, flash chromatography on silica gel (3:1 (v/v), hexanes/EtOAc) afforded **27a** as a viscous oil (98 mg, 90%, 5:1 dr). Major isomer: R_f (50% EtOAc/hexane) = 0.43; $[\alpha]_D^{25}$ −4.1 (*c* 2.3, CH_2Cl_2); For the remaining spectral data see Section 4.42.

4.44. (2*S*,3*R*,4*S*,5*S*)-5-(Ethoxycarbonyl)-1-(benzyloxy)-3-fluoro-4,5-dihydroxypentan-2-yl 3-methylbenzoate (28a)

Into a 50 mL round bottomed flask were added 4 mL of *t*-BuOH, 4 mL of water, $K_3Fe(CN)_6$ (370 mg, 1.13 mmol), K_2CO_3 (155 mg, 1.13 mmol), $MeSO_2NH_2$ (36 mg, 0.38 mmol), $(DHQD)_2PHAL$ (6.1 mg, 7.9 μmol, 2.1 mol %), and OsO_4 (1.9 mg, 7.5 μmol, 2 mol %). The mixture was stirred at rt for about 15 min and then cooled to 0 °C. To this solution was added **14a** (150 mg, 0.38 mmol) and the reaction was stirred vigorously at 0 °C overnight. The reaction was quenched by the addition of solid sodium sulfite (50 mg) at rt. EtOAc (15 mL) was added to the reaction mixture and after separation of the layers, the aqueous phase was further extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (3:1, hexanes/EtOAc) afforded **28a** as a viscous oil (130 mg, 80%, 3:1 dr). Major isomer: R_f (50% EtOAc/hexane) = 0.42; $[\alpha]_D^{25}$ 7.2 (*c* 1, CH_2Cl_2); IR (thin film): 3456, 3032, 2924, 1725, 1608, 1590, 1455, 1369, 1276, 1200, 1101, 1026, 744 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.86 (m, 2H), 7.29 (m, 7H), 5.53 (dddd, *J* = 15, 6.6, 4.2, 2.4 Hz, 1H), 5.06 (ddd, *J* = 47.4, 6, 4.8 Hz, 1H), 4.61 (d, *J* = 12 Hz, 1H), 4.56 (d, *J* = 12 Hz, 1H), 4.40 (dd, *J* = 4.2, 2.4, 1H), 4.29 (q, *J* = 7.2, Hz, 2H), 4.16 (ddd, *J* = 21, 4.8, 2.4, 1H), 3.94 (ddd, *J* = 10.8, 6 Hz, 1H), 3.81 (dd, *J* = 10.8, 6.6 Hz, 1H), 3.22 (d, *J* = 4.2 Hz, 1H), 2.97 (d, *J* = 7.2 Hz, 1H), 2.40 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.5, 165.7, 138.2, 137.6, 134.1, 130.3, 129.3, 128.4 (2C), 128.3, 128.2, 127.8, 127.6, 126.9, 91.2 (d, *J* = 175.9 Hz), 73.4, 70.7 (d, *J* = 7.9 Hz), 70.6 (d, *J* = 11.6 Hz), 67.2 (d, *J* = 4.6 Hz), 62.3 (d, *J* = 28.3 Hz), 60.3, 21.1, 14.0; CIMS calculated for $[C_{15}H_{27}FO_7+Na]^+$: 457.1633. Found: 457.1635.

4.45. (2*R*,3*R*,4*S*,5*S*)-Ethyl 6-(benzyloxy)-4-fluoro-2,3,5-trihydroxyhexanoate (19a)

To a solution of **27a** (100 mg, 0.23 mmol) in EtOH (2 mL) was added 10% HCl in EtOH (0.3 mL) and the mixture was heated at reflux for 24 h. Then EtOH was removed under reduced pressure and flash chromatography on silica gel (1:1, hexanes/EtOAc) afforded **19a** as a viscous oil (55 mg, 75%). R_f (60% EtOAc/hexane) = 0.20; $[\alpha]_D^{25}$ −2.1 (*c* 2.7, CH_2Cl_2); IR (thin film): 3402, 3033, 2922, 2862, 1736, 1496, 1453, 1365, 1216, 1072, 1026, 811 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.33 (m, 5H), 4.60 (ddd, *J* = 46.6, 8.4, 6.6 Hz, 1H), 4.58

(br s, 2H), 4.39 (dd, $J = 6.6$, 1.2 Hz, 1H), 4.29 (q, $J = 7.2$ Hz, 2H), 4.22 (ddd, $J = 13.2$, 6.6, 1.2 Hz, 1H), 4.14 (dddd, $J = 16.2$, 6.6, 6, 5.4 Hz, 1H), 3.72 (dd, $J = 9.6$, 6 Hz, 1H), 3.66 (dd, $J = 9.6$, 6.6 Hz, 1H), 3.49 (d, $J = 5.4$ Hz, 1H), 3.33 (d, $J = 6.6$ Hz, 1H), 3.09 (d, $J = 4.8$ Hz, 1H), 1.30 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 172.8, 137.3, 128.5 (2C), 128.0, 127.8 (2C), 89.1 (d, $J = 175.4$ Hz), 73.7, 71.8 (d, $J = 25.5$ Hz), 71.2 (d, $J = 24.7$ Hz), 70.0 (d, $J = 3.5$ Hz), 69.9 (d, $J = 5.8$ Hz), 62.1, 14.1; CIMS calculated for $[C_{15}H_{21}FO_6+Na]^+$: 339.1214. Found: 339.1217.

4.46. (3*R*,4*R*,5*R*,6*S*)-6-((Benzyloxy)methyl)-5-fluoro-tetrahydro-3,4-dihydroxypyran-2-one (25a)

To a solution of **19a** (50 mg, 0.50 mmol) in benzene (1 mL) was added pyridinium toluenesulfonate (1.5 mg, 5.7 μmol, 5 mol %), and the mixture was heated at reflux for 5 h. The reaction was cooled to rt and quenched by the addition of saturated aqueous sodium bicarbonate (0.5 mL). The aqueous layer was extracted with ether (3 × 10 mL). The organic layer was washed with brine (10 mL) and dried with anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (1:1, hexanes/EtOAc) afforded **25a** as a viscous oil (28 mg, 90%). R_f (60% EtOAc) = 0.19; $[\alpha]_D^{25}$ −1.4 (*c* 1.5, CH_2Cl_2); IR (thin film): 3404, 3032, 2872, 1742, 1497, 1454, 1367, 1200, 1103, 1025, 957, 917 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.30 (m, 5H), 5.01 (ddd, $J = 49.2$, 1.8, 1.2 Hz, 1H), 4.75 (dd, $J = 10.8$, 1.8 Hz, 1H), 4.57 (d, $J = 12$ Hz, 1H), 4.50 (ddd, $J = 16$, 10.8, 1.2 Hz, 1H), 4.47 (d, $J = 12$ Hz, 1H), 4.37 (dddd, $J = 16.8$, 10.8, 2.4, 1.8 Hz, 1H), 3.74 (br s, 1H), 3.68 (ddd, $J = 10.8$, 4.2, 2.4 Hz, 1H), 3.65 (dd, $J = 10.8$, 2.4 Hz, 1H), 3.26 (br s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 171.7, 136.7, 128.5 (2C), 127.9, 127.8 (2C), 90.1 (d, $J = 177.6$ Hz), 79.3 (d, $J = 23.7$ Hz), 73.8, 69.3, 69.2 (d, $J = 12.1$ Hz), 68.5 (d, $J = 10.4$ Hz); CIMS calculated for $[C_{13}H_{15}FO_5+Na]^+$: 293.2434. Found: 293.2437.

4.47. (3*R*,4*R*,5*S*,6*S*)-6-((Benzyloxy)methyl)-5-fluoro-tetrahydro-3,4-diacetoxypyran-2-one (26a)

To a solution of **25a** (20 mg, 0.07 mmol) in CH_2Cl_2 (2 mL) were added excess Ac_2O (20 μL, 0.17 mmol), pyridine (0.30 μL, 0.34 mmol) and a catalytic amount of DMAP (1 mg, 5 mol %). The reaction was stirred for 2 h, after which 10 mL of ether and 10 mL of NH_4Cl were added to remove excess base. The organic layer was washed with 5 mL $CuSO_4$ solution, 5 mL brine and the aqueous layer was further extracted with ether (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed in vacuo. The crude product was purified by flash chromatography on silica gel (4:1, hexane/EtOAc) to yield **26a**. (24 mg, 95%) as a viscous oil. R_f (40% EtOAc) = 0.37; $[\alpha]_D^{25}$ 4.9 (*c* 2, CH_2Cl_2); IR (thin film): 2872, 1751, 1454, 1373, 1216, 1103, 1057, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.33 (m, 5H), 5.75 (ddd, $J = 16.8$, 10.2, 2.4 Hz, 1H), 5.69 (dd, $J = 10.2$, 2.4 Hz, 1H), 5.14 (ddd, $J = 48$, 2.4, 2.4 Hz, 1H), 4.80 (dddd, $J = 16.8$, 4.8, 2.4, 2.4 Hz, 1H), 4.64 (d, $J = 12$ Hz, 1H), 4.53 (d, $J = 12$ Hz, 1H), 3.74 (ddd, $J = 10.8$, 4.8, 2.4 Hz, 1H), 3.71 (dd, $J = 10.8$, 2.4 Hz, 1H), 2.15 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 169.9, 169.6, 165.4, 136.5, 128.5 (2C), 128.1, 127.8 (2C), 88.7 (d, $J = 160.9$ Hz), 78.7 (d, $J = 20.8$ Hz), 74.0, 68.7 (d, $J = 16.8$ Hz), 67.8, 67.0, 20.6, 20.4; CIMS calculated for $[C_{17}H_{19}FO_7+Na]^+$: 377.3167. Found: 377.3169.

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